WCVM Student Research Writing | **2011-2017**





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A selection of articles written by students who participated in the WCVM Undergraduate Summer Research and Leadership program from 2011 to 2017.



Cover: Horses walk the beach on Sable Island. **Market Methods and Security of Security Content in Content Secure Provided For Content Security Content Secur**

Isolated horses offer insight into virus

A horse stands on top of a sandy dune, his coat matted and eyelids lowered against the fierce wind. Ocean waves crash against the shoreline to his right, outlining the crescent-shaped wedge that is Sable Island, home to one of the last wild horse populations in Canada.

July 12th, 2017 | By Jane Westendorf

The conditions surrounding Sable Island horses have long interested scientists, offering them a glimpse into natural herd hierarchy, island ecology and genetic drift. A team at the Western College of Veterinary Medicine (WCVM) is particularly interested in what this herd may be harbouring within their thick, weatherbeaten skin.

For the past few years, WCVM veterinary pathologist Dr. Bruce Wobeser has been exploring the connection between papillomavirus (PV) and the development of skin tumours in horses. PV is a virus with many strains that affects most animal species. Human papillomavirus (HPV) is the most well known as the cause of cervical cancer in women.

"PV is a virus that affects the skin and causes rapid growth of skin cells. That growth can become transformed into a cancer and that's what we think we see in human cervical cancer, for example,"Wobeser explains.

"Most of the time, when people or animals get infected, they develop an immune response and nothing happens. Rarely that immune response is delayed and they develop a papilloma or a wart, and even more rarely, that immune response is so delayed that you get a tumour or cancer development. So while lots are exposed, very few develop cancer."

Wobeser and his graduate student, Dr. Sarah Greenwood, have been working together to determine how common the virus is in the domestic horse population. When Dr. Todd Shury, a veterinarian with Parks Canada who is based at the WCVM, planned a trip to Sable Island, N.S., this spring, a unique opportunity presented itself to Wobeser.

"I approached Bruce and said, 'I know you have a research interest in skin diseases in horses. Do you want some samples?"" explains Shury, whose trip to Sable Island was supported by Dr. Phil McLoughlin, a researcher in the University of Saskatchewan's biology department. "That's the great thing about working in a vet college. I can go have these hallway conversations with people. A lot of research projects start that way."

Wobeser was particularly interested in the status of PV in the island's horses.

"We were working on Sarah's project on prevalence," says Wobeser. "It occurred to me that Sable Island was a unique



environment and so it would make a nice contrast with this wild, free-ranging horse population to see what the natural history of the disease would be like without human intervention. If it's different, [or] if it's not different."

Ancestors of the Sable Island horses were brought to pasture on this small island back in the mid-1700s. Now numbering upwards of 500 head, the feral horses have thrived for more than 200 years among the fog and the sandy dunes.

"It's a really unique place," Shury says. "It's such a simple ecosystem: a 40-kilometre long sandbar, limited vegetation and one herbivore. And no predators."

Harsh winter conditions and deep sand have left these animals with shaggy coats and characteristically curved hooves, but no overt disease appears to affect the herd.

During his time on the island this spring, Shury collected skin samples from 25 equine carcasses found on the sandy beaches of Sable Island. WCVM parasitologist Dr. Emily Jenkins and several graduate students from McLoughlin's lab group helped him with the task.

The samples were then put into preservative and brought back to Saskatoon where Wobeser's team fixed them into blocks of paraffin wax.

The researchers began the challenge of hunting for potential traces of PV in the samples — but identifying the virus was not a simple task. Without any reliable external indicators of disease to work from, the team set out to isolate the presence of viral DNA in the Sable Island equine tissue samples.

Through a series of chemical steps, the research team successfully extracted and replicated DNA in the lab. They used another protocol to test this DNA for the virus with primers specially designed to recognize a common sequence in PV.

The team did not find papillomavirus in any of the Sable Island samples. On a small island with a limited population, Wobeser says it's possible that there is no PV.

"Whether there was nobody shedding or nobody had PV when they arrived on the island ... or whether it's such a small group that everyone has been infected and has developed an immune response to it and therefore there's no susceptible animals anymore — that's possible, too."

Since the samples were collected from horses that died of exposure or old age, the project's small sample size may not be representative of the entire population of the island.

Using a statistical algorithm based on data collected by this study, the maximum prevalence that PV could exist within the herd is 13.7 per cent. Compared to studies on the local domestic population in Western Canada where PV is estimated to occur in about 30 per cent of horses, PV appears to occur at a significantly lower rate in the Sable Island herd.

This difference could be due to any number of reasons surrounding the wild herd and warrants further investigation.

Regardless, this Sable Island project is another step towards understanding PV in horses. Through continued research, the team at WCVM hopes to shed light on a virus that affects a wide range of species — including humans.

Jane Westendorf of Mission, B.C., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2017. She was also the Townsend Equine Health Research Fund summer research student and a Merial Veterinary Scholar. Jane's story is part of a series of stories written by WCVM summer research students.

Tales from the tundra: research in Nunavut

On an island in the middle of Karrak Lake in northern Nunavut, there's a small field camp located 300 kilometres from the nearest civilization. It's a spectacular place where you can experience three seasons in two months and never see the sun set the entire time.

December 13th, 2016 | By Keaton Schmidt

During the summer of 2016, I spent two months at this isolated camp while conducting research on Arctic fox under the supervision of Dr. Emily Jenkins, a professor in the Western College of Veterinary Medicine's (WCVM) Department of Veterinary Microbiology.

Environment Canada maintains the field camp, which is located on a colony that includes over a million nesting lesser snow geese and Ross's geese within the Queen Maud Gulf Migratory Bird Sanctuary. Although the research focus was initially on these geese, Arctic foxes were eventually added to that mandate; Dr. Jenkins and her research team became involved in studying the health of these Arctic foxes.

Accompanied by a group of Environment Canada researchers and volunteers, I arrived at camp on May 20 in a Twin Otter airplane that flew from Cambridge Bay. Our first task was to dig out the cabins from some very deep snow, and one was even partly filled – thanks to a bear break-and-enter over the winter.

For the rest of May and early June, I worked alongside my assistant Audrey Tremblay and biologist Gustaf Samelius who has many years of experience working with the foxes. We trapped adult foxes on various dens around the colony – the same den sites that the foxes have used for centuries. We baited the traps with sardines — irresistible to winter-hungry foxes — and watched from tents placed about 100 metres away. Once the foxes were trapped and sedated, I collected blood and fecal samples while Gustaf placed ear tags on the animals as part of a long-term mark-recapture study.

Our work is part of an ongoing study on the protozoan parasite *Toxoplasma gondii* in the Karrak Lake foxes. Commonly known as the "cat litter" parasite, it has an unusually high prevalence in some Arctic wildlife and in people despite the absence of cats – the definitive host of the parasite – above the tree line.

"Toxoplasmosis affects Inuit in Nunavut and Nunavik (northern Québec) at a rate [of] at least two to four times that of the North American average," explains Émilie Bouchard, a PhD candidate at the WCVM. "Toxoplasma gondii can cause problems in the immunocompromised and in the fetuses of women infected for the first time during their pregnancy, and [the parasite] is considered a threat to conservation for some wildlife such as sea otters."



C Keaton Schmidt

The blood samples that I collected from the adult foxes and their pups were tested for exposure to T. gondii, adding to information gathered over many years of monitoring this population of marked individual animals. In 2016, none of the pups or their mothers were positive for exposure to T. gondii, consistent with previous findings that young pups can get the parasite from their mothers even before they are born rather than from food consumed around weaning.

Team members also analyzed the fecal samples to characterize the gastrointestinal parasite fauna in the Karrak Lake fox population. As climate change causes rapid changes in the Arctic environment, the data gathered this year will be used for future comparisons of parasite diversity.

While Jenkins and her team members have collected data on gastrointestinal parasites in the foxes in past years, this was the first year that they investigated parasite fauna of the juvenile foxes. Coccidian oocysts were present in 82 per cent of samples from fox pups, as well as roundworms and hookworms in six per cent of pup samples. These parasites are likely transmitted from adult foxes to pups through fecal contamination, and they could have an impact on pup health.

I also tested fecal samples deposited by adult foxes that I collected opportunistically from dens. With these samples, I could compare the 2016 parasite diversity to that of past years – a means of investigating the variations that have occurred in the foxes' gastrointestinal parasites over time.

Future studies could simultaneously monitor environmental factors (such as climate) and ecological factors (such as fox density or movements of migratory species) to determine what might be affecting the parasites found in the foxes.

In early June as the snow began melting and the geese began to arrive on the colony to nest, it was quite spectacular to see the landscape transform so rapidly and dramatically. What began as barren, frozen Arctic was quickly overrun with nesting geese as well as shorebirds, long-tailed ducks and beautiful king eiders.



In time the tundra also became inundated with adorable goslings. This is the best part of the summer for foxes as the geese and their eggs and goslings present a significant food source for them. Unfortunately, that meant the foxes were no longer interested in our sardine bait, so that was the end of our season of adult fox trapping.

The next – and most exciting – step of our research work was to trap fox pups. We found pups at three dens, and I placed trail cameras on the dens to watch the young foxes' first steps into the wider world. It was fortunate that we found pups this year as fox breeding is largely dependent on lemming populations, which follow a cyclic pattern of peaks and crashes. Nursing pups had little interest in food bait, but since they were very curious and naïve, we simply used objects such as hanging bones or feathers in the trap to stimulate their curiosity and lure them in.

Even though we had to tolerate obscene numbers of mosquitoes, sitting outside all evening watching fox pups run around, wrestle and play was a pretty great job. They are extremely cute and always highly entertaining.

My two months spent in the Arctic were hugely rewarding – an opportunity to experience nature's beauty while carrying out important work that can benefit both the environment and the human population.

"We are trying to determine how does Toxoplasma gondii get in the Arctic, transmit in Arctic food webs and what effects does it have on wildlife and human health," says Bouchard. "It is important to understand how it is introduced and transmitted, for both wildlife and human health."

Funding for this project was supplied by the WCVM's Interprovincial Undergraduate Summer Student Research Program, Natural Sciences and Engineering Research Council of Canada (NSERC), ArcticNet National Centres for Excellence, and the Canadian Foundation for Innovation Leaders Opportunity Fund infrastructure funding for the Zoonotic Parasite Research Unit.

Keaton Schmidt of Saskatoon, Sask., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2016. Keaton's story is part of a series of stories written by WCVM summer research students.

Could brushes give clues to cattle health?

Could the grooming behaviours of dairy cows be used to tip off the farmer that a cow's not feeling well?

December 6th, 2016 | By Deanna Larsen

That's the question researchers at the Western College of Veterinary Medicine (WCVM) are looking to answer in a trial that's currently underway at the University of Saskatchewan's Rayner Dairy Research and Teaching Facility.

"We're investigating dairy cow use of automatic brushes," explains Joe Stookey, a cattle behaviourist and professor at the WCVM. "What we are looking for specifically is the pattern of their use — whether they use it daily, how frequently they use it, and whether that use changes with lameness or illness."

Automatic brushes are becoming a standard in free stall dairy barns and are available to the cows whenever they're in their home pens. Once the brush has been activated by the cow, it begins to spin and provides grooming opportunities for those hard-to-reach places such as the back, hindquarters and tail.

By pairing an individual lameness assessment with an observational study of each dairy cow's interaction with the brush, the study seeks to characterize the cow's daily brush use, looking for any indications of early lameness.

"If they do use the brushes every day and then that changes they start using it less or more during a lameness or injury — you could use that as an early detector," explains Stookey.

Looking for lameness in every cow in a dairy herd is time consuming, and the stoic nature of cattle often makes subtle lameness challenging to detect. As a result, lame cows can often go undetected until their lameness has progressed and become more severe. Since severe lameness is often difficult to resolve and more likely to become a chronic problem, early detection and treatment are key.

To carry out the project, the researchers installed surveillance cameras in the barn so they could have an around-the-clock record of the cows using the brushes. The team also learned how to visually assess the movement of cattle so they could determine when a cow is sore or lame. A cow that has a sore foot will shift its weight and try to take weight off that foot, resulting in a limp.

As automated detection is gaining popularity in the dairy industry, activity monitors are widely used to detect cows coming into heat for breeding purposes. Sensors in milking systems are also used to provide information about milk quality and udder health.

That's why it's not such a stretch of the imagination to envision that the observation of automatic brush use could be another step toward improved animal care. If the producer is alerted whenever a change in brush use occurs, there's a greater chance of detecting lameness problems before they become severe.



If a dairy cow uses the automatic brushes less or more during a lameness or injury, the devices could be an early detector.

Deanna Larsen of Edmonton, Alta., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2016. Deanna's story is part of a series of stories written by WCVM summer research students.

Tracking dairy heifer parasites in SK

Standing in the middle of a pasture and melting in the July heat, following a group of heifers around the field collecting manure samples – it's all part of Haley Scott's glamorous research job.

May 11th, 2017 | By Traci Henderson

Scott's interest in cattle stems from growing up on a beef farm near Lacombe, Alta. Now a graduate student pursuing a Master of Science (MSc) degree at the WCVM, she's part of a research group that's investigating the prevalence of gastrointestinal nematodes – parasites – in Saskatchewan dairy cattle.

Gastrointestinal nematodes are present in dairy cattle worldwide, and their negative impact on production in dairy herds has been well documented. They result in large economic losses and although recent information is lacking, it has been estimated that parasites cost the U.S. cattle industry \$2 billion a year due to lost productivity. Scott and her research team are working to obtain baseline data about the number and species of gastrointestinal nematodes present in Saskatchewan dairy heifers of breeding age. They're evaluating heifers on six farms that are being pastured for the summer.

The cost of raising heifers is one of the largest expenses for a dairy operation. Since these animals have a developing immune system and no previous exposure to parasites, they're at an increased risk of developing parasitic infection. These infections can also affect their growth rate, affecting their lifetime productivity.





ey Scott works with dairy cattle in the field.

In the past, producers have used anthelmintic drugs (dewormers) to control parasite loads in their animals, but there are increasing reports of anthelmintic resistance that's affecting livestock industries worldwide. Recent data from the U.S. indicates that internal parasites in beef cattle are developing resistance to ivermectin and benzimidazoles, the most commonly used anthelmintic drugs.

"With the looming threat of anthelmintic resistance, it is important for producers to understand the risks of parasitism and the opportunities and benefits of managing herds to slow the spread of resistance," says Scott.

Since there's no information on the prevalence of gastrointestinal nematodes in Saskatchewan dairy herds, it's difficult to evaluate the presence or the extent of anthelmintic resistance in the region or even to know to what extent and with what parasite species dairy heifers are infected with.

Given the well-documented impact of internal parasite burden on cattle health and production as well as the increase in anthelmintic drug resistance, it's critical for researchers to close this knowledge gap.

Once researchers have determined the level of parasitism and anthelmintic resistance that exists in growing dairy heifers in Western Canada, dairy producers can act on that information.

By developing economically sound and sustainable control practices, they can decrease the impact of internal parasites on production and limit the development of anthelmintic resistance.

Traci Henderson of Gainsborough, Sask., is a third-year veterinary student. Her research was funded by the WCVM Interprovincial Summer Student Research Program. Traci's story is part of a series of articles written by WCVM summer research students.

Can a breast cancer drug benefit cattle?

Can a drug that's proved useful for humans be of value to the beef and dairy cow industry?

May 18th, 2017 | By Brittany Davis

That's a question Dr. Gregg Adams and a team of researchers at the Western College of Veterinary Medicine (WCVM) are hoping to answer.

Adams and his team are investigating the effects of letrozole, a non-steroidal drug commonly used in human medicine to treat infertility and breast cancer in women. Their research focuses on letrozole's effects on ovarian function and its possible use for synchronizing the reproductive cycles in cattle. Being able to trigger the synchronization of estrus or heat is useful because it means that the females can all be bred at approximately the same time.

Synchronizing reproductive cycles is an important tool in the cattle industry because it allows cattle producers to apply advanced reproductive technologies such as fixed-time artificial insemination and embryo transfer. By using these technologies, they can operate more efficiently and profitably.

Letrozole was commonly used for treating breast cancer, but when researchers discovered that the drug had ovarian effects which improved fertility in women, they developed a bovine model aimed at understanding more about its function. That model led to their realization that letrozole could also benefit the cattle industry.

Letrozole is an aromatase inhibitor; that means it blocks the enzyme responsible for converting testosterone into estrogen. The drug prolongs the lifespan of the dominant follicle in the ovary, resulting in the delay of ovulation.

"It prevents the follicle from producing what it wants to produce and that's estrogen," says Adams, a veterinary professor who specializes in theriogenology. "Due to low levels of estrogen, there is no suppression of luteinizing hormone released from the pituitary gland in the brain so it can continuously feed the dominant follicle, causing it to grow."

Although it's unknown whether the dominant follicle can be maintained this way indefinitely, researchers discovered that they could delay ovulation by administering this drug for a short period of time - making it a useful tool for synchronization in cattle.

Traditionally, synchronization for fixed-time artificial insemination was done using a combination of estrogen and progesterone. Artificial insemination is a technique where semen is collected from a bull and then manually inserted directly into the uterus of a cow.

But less than six per cent of North American beef cattle producers use artificial insemination, and in Adam's view that



O Brittany Davis

low rate represents a lost opportunity for the cattle industry.

"Producers are missing out on two important things: condensing the calving season and the opportunity to use high quality genetics," says Adams.

"In the early '90s we developed a steroid approach for synchronization in cattle and it was awesome; it took off across the world, particularly in South America. The South Americans really showed us how well artificial insemination works and how it is an important part of the beef business."

By taking advantage of advanced reproductive technologies, South America can produce high-quality beef more efficiently. The rest of the world has been slower to implement artificial insemination in their cattle herds, partly due to the stricter regulations on the use of steroids in food production animals.

While estradiol is commonly used for synchronization in South America, its use has been banned in the European Union, Australia and New Zealand, and there are increasing restrictions on its use in North America.

These restrictions result from the increasing controversy surrounding the use of hormones in food production animals due to potential health and environmental concerns.

"The residue created by the estradiol synchronization protocol is negligible, but perception rules, and the perception is that there are too many estrogens floating in the environment and we need an alternative," explains Adams.

Alternative, non-steroidal methods for synchronization are available, but none have had great success. However, letrozole has the potential to meet consumer demands. It's a non-steroidal



drug that's been proven safe for humans, and it's been approved by the FDA for treatment of breast cancer and infertility in women.

Another benefit of letrozole: it's easy to use. Producers can administer a dose using a minimally invasive intravaginal device that allows for prolonged drug release and reduces animal stress and handling, as opposed to protocols that involve multiple injections. The device also allows for immediate removal of the drug source once the medication period is up.

Letrozole could prove to be a very useful tool for the dairy and beef cattle industries. Right now there's a lack of products that can generate synchronization, and with an expanding market this drug has a lot of potential.

Although letrozole is an exciting advancement for the cattle industry that promises to provide a consumer-friendly, costefficient alternative to current synchronization methods, Adams is cautiously optimistic.

"With research you have to be patient and take a step-by-step approach and that's what we are doing," he says.

Brittany Davis of Saskatoon, Sask., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2016. Brittany's story is part of a series of articles written by WCVM summer research students.

Advanced treatment for canine cancer

For a pet owner, the worst news in the world is hearing that your furry best friend has cancer.

June 20th, 2017 | By Jordyn DeWalt

That was exactly the case for dog owners Lisa and Chris.

"It was the worst day ever," says Lisa, recounting the day they found out their 12-year-old Boston terrier Oakley had a nasal tumour.

"We'd go to bed at night and he'd be lying there and gasping for air; he wouldn't sleep because he wasn't able to breathe," says Chris. "He was so fatigued because he wasn't sleeping that he would just be standing there and would fall over because he was so tired."

While cancer of any type is hard to treat, nasal tumours cause added grief for veterinary oncologists because of all the important structures nearby, particularly the eyes and the brain. They're perhaps the most important tissues to consider because the side effects of radiation can be life altering.

Too much radiation to the eyes can cause long-term cataracts or blindness, and too much to the brain can cause seizures and other neurological changes. To avoid the side effects but still treat this small area, oncologists need to use a very targeted radiation treatment — and that's where the highly-focused beams and on-board imaging capabilities of newer linear accelerators come in.

Stereotactic radiation therapy (SRT) is a type of radiation therapy that uses highly-focused beams and on-board imaging – and the entire dose of radiation is delivered in one to five doses, usually three in veterinary medicine. SRT is delivered over a period of days instead of the weeks needed for conventional radiation therapy, thus reducing the amount of time patients need to be in the hospital and under general anesthetic.

Because the anesthetic episodes are reduced from approximately 20 to only three, treatment can now be made available to those patients unable to handle many repeated anesthetic episodes. In addition, out-of-town owners are able to reduce their stay in Saskatoon from a month to less than a week.

"You are giving a curative dose of radiation but only in three fractions," explains Dr. Monique Mayer, a board-certified veterinary radiation oncologist at the Western College of Veterinary Medicine (WCVM). "New technology allows us to really precisely deliver the dose of radiation and adjust the fields to the patient position in real time. We can give it so accurately that we are avoiding the normal tissues, so we can give those high doses." That means the immediate side effects are also greatly reduced for the patients that had previously experienced severe effects when conventional radiation therapy was used to treat nasal tumours.



"We always accepted with conventional dose [radiation

therapy] that nasal tumour patients were probably the worst patients for side effects because their whole face and a good portion of their mouth was affected," explains Mayer. "That is the biggest difference I think for the patient – less side effects or very limited side effects [with SRT]."

Researchers at the WCVM are now investigating how the outcome of SRT compares with conventional radiation therapy for nasal tumours. Since canine nasal tumours are most commonly treated with radiation alone, the scientists can readily compare the results and side effects of SRT to those of the older treatment methods.

If SRT is shown to provide at least the same level of tumour control with comparable or decreased side effects to healthy tissue, it may become the new treatment of choice for many types of cancer.

When Lisa and Chris look back, they're convinced that SRT was the best option for treating Oakley's nasal tumour. Thanks to the dedicated team at the WCVM Veterinary Medical Centre, their spunky combine-riding, shoe-stealing, affectionate Boston is back to his old ways of playing with his sister Nala.

"If we weren't going to treat with radiation, [the clinicians at the VMC] said we should say our goodbyes," recalls Lisa. "Seeing him now, he is doing so well! We totally did the right thing, he wasn't ready to go."

Jordyn DeWalt is a fourth-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2016. Jordyn's article is part of a series of stories written by WCVM summer research students.

New device gives healing horses a lift

It's 8 a.m., and I'm all set for a long day of filling out paperwork for my summer job as a student researcher at the Western College of Veterinary Medicine (WCVM).

March 1st, 2016 | By Alison Williams

Less than an hour later I'm suturing up an eight-inch laceration on the shoulder of "Mama," one of our research horses, in the WCVM Veterinary Medical Centre's equine treatment room.

As I'm beginning to learn, horses seem to love finding creative ways of injuring themselves. Luckily for Mama, several dozen stitches and a dose of antibiotics will help her to heal up nicely.

But for many other equine injuries such as leg fractures, there is little hope of recovery — until now.

A team of researchers has partnered with RMD Engineering, a local Saskatoon engineering and manufacturing company, to design and build a one-of-a-kind robotic lift system. The lift will help rehabilitate horses suffering from acute injuries and other musculoskeletal problems by providing mobility, weight distribution and support.

The team's leader is Dr. Julia Montgomery, a large animal internal medicine specialist at the WCVM and my research supervisor. She and her colleagues are combining their expertise to find a solution for horses that sustain life-threatening injuries.

Research team members further include professors from the University of Saskatchewan's College of Engineering, an equine biomechanics specialist from the university's College of Kinesiology and Montgomery's husband James, a board-certified veterinary radiologist.

RMD Engineering owner Jim Boire says his company is built around the desire to find solutions to seemingly insurmountable problems. He has been involved with many other innovations at the U of S including the WCVM's bovine tilt table, a hydraulic device for lifting cows, and a large animal positioning system for the Canadian Light Source synchrotron.

"We're driven by helping people fix problems," says Boire. "That's what we like doing and that's really what our company does."

The idea for the equine lift originated from a similar lift system that RMD designed to help people with multiple sclerosis.

"When we meet people like James and Julia [Montgomery] that we get to work with, it just makes us smarter. We really push hard to make it a team, we run things as projects and everybody has their role," says Boire.

Hundreds of horses are fatally injured and euthanized every year in North America due to racetrack injuries, and a large majority of these injuries are skeletal fractures. But even horses that are used for pleasure riding can break a leg.

After a horse undergoes surgery to fix a leg fracture, it's normally confined to a stall and given medication to alleviate the pain.



The equine lift in use. This lift holds the potential to help horses recover more easily from injuries.

However, due to a horse's heavy weight and its strong flight response, recovery from musculoskeletal problems is fraught with complications and secondary issues such as supportinglimb laminitis – as was the case with the famous racehorse, Barbaro.

The Kentucky Derby winner shattered his right hind fetlock while racing in the Preakness Stakes on May 20, 2006. Equine surgeons successfully repaired his leg, but eight months later, Barbaro was euthanized after developing laminitis in his other feet.

Veterinarians regularly use slings to help support injured horses, but current designs significantly limit the animals' normal activity and support all of their weight on the thorax and abdomen. This leads to further problems because of compression on the lungs and development of pressure sores.

With the lift system, Montgomery says clinicians can reduce and redistribute the weight the horse is carrying dynamically. The system allows the animal to be mobile with its weight partially or fully supported by the lift.

"If we want to, we can allow the horse to move around so we don't have these issues with muscle wasting," says Montgomery. She adds that this function of the lift will also allow for more controlled rehabilitation of horses.

Leg fractures are one of the most common injuries that will benefit from this new technology, but the lift can also be used with equine patients suffering from other musculoskeletal and neurological problems.

Montgomery and her research team have been conducting initial trials with the horse lift. First, they're examining how three healthy horses — including Mama — tolerate hanging out for extended periods of time in the sling and prototype lift system. Next, they will use it with equine patients that have sustained limb fractures and would otherwise be euthanized. These trials will help them determine how the lift affects the horse's behaviour and basic physiological parameters such as muscle enzymes and blood flow. They will also monitor the animals for pressure sores caused by the sling.

The research team believes that the unique horse lift will decrease the pain of recovery for equine patients, shorten their recovery periods and reduce complications. As a result, it will also help to decrease treatment costs and reduce emotional distress for both the owner and horse.

"[The lift] really provides a novel and unique solution to a very frustrating problem that currently doesn't have a solution," says Montgomery.

Alison Williams of Calgary, Alta., is a third-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2015. Alison's story is part of a series of stories written by WCVM summer research students.



The equine lift research team, from left: students Alison Williams, Louisa Belgrave, Dr. Julia Montgomery and Dr. James Montgomery.

Cause of bovine digital dermatitis elusive

For more than four decades, a painful disease has plagued dairy cattle – and a team of Western College of Veterinary Medicine (WCVM) researchers are rethinking the causative agent.

February 16th, 2016 | By Larissa Goldsmith

Since 1974 when the first case was identified in Italy, bovine digital dermatitis (BDD) or heel wart has spread to almost every dairy-producing country in the world. The disease has caused both animal welfare and economic issues for the international dairy industry.

"It is essential to determine the causative agent of digital dermatitis so that we can develop new, more effective treatment and control strategies," says Dr. Chris Luby, an assistant professor in the WCVM's Department of Large Animal Clinical Sciences who is part of the research team.

BDD is an infectious, proliferative lesion that develops most commonly on the skin immediately above the horn of the hoof, on the back feet of dairy cattle. It is usually located in between the bulbs of the heel or on the skin between the clefts of the hoof. It causes extreme pain resulting in lameness. As a result of the lameness, cattle don't rebreed as easily, milk production decreases, animals are culled sooner and maintenance costs per cow increase due to treatment costs.

Researchers originally thought that Treponema bacteria caused this disease. However a recent discovery from Iowa State University indicates that early lesions have low numbers of Treponema bacteria while advanced lesions have much greater numbers of the bacteria.

Scientists now suspect that BDD is a polybacterial disease (multiple organisms acting collectively to incite disease progression). Research has shown that bacterial DNA is predominant at all phases of the disease with almost no viral or fungal DNA present — reinforcing the theory that the disease's main causative agent is bacteria.

Multiple species also seem to be susceptible to this condition: a similar disease has been found in beef cattle, sheep, goats and elk. In all of these species, researchers have found high numbers of Treponema bacteria in the lesions just as they are in dairy cattle.

The WCVM research team, in collaboration with Iowa State University, is looking at the biological aspects of the disease by collecting samples from the heel skin of animals with and without the disease on dairies that currently have BDD cases. Researchers are also looking at samples from a dairy herd that has never had BDD — an important part of their study.

It is difficult to find dairies in North America that do not have BDD, so being able to compare samples to a dairy that is free of BDD gives the team a unique look at the different bacteria present or absent.



Maria Epp prepares a cow's hoof before taking a biopsy sample.

This foot is showing a classic advanced stage of

digital dermatitis in a dairy cow. Here it has been cleaned up to take a biopsy of the lesion to be able to identify the bacteria that are present in it.

Researchers will sequence DNA in these hoof samples to determine the bacteria present in both infected and noninfected animals as well as animals with no previous exposure. By comparing the results from these different groups of animals, researchers can look for any differences in the bacterial populations.

When researchers can determine a definitive causative agent for the disease, the next step is to develop a vaccine for the disease along with preventive measures that can be implemented by dairy producers on their farms.

This research project is financially supported by the Saskatchewan Agriculture Development Fund, Western Economic Diversification and SaskMilk.

Larissa Goldsmith of Baldur, Man., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2015. Larissa's story is part of a series of stories written by WCVM summer research students.

Equine drug study leads to rule change

Results from a Western College of Veterinary Medicine (WCVM) study have led to a nation-wide change in Equine Canada-sanctioned competition rules regulating the use of the drug firocoxib in performance horses.

April 14th, 2016 | By Jessica Semper

The national equine sport organization's rule change regarding firocoxib's use came into effect on Jan. 1, 2016.

Firocoxib is a non-steroidal anti-inflammatory drug (NSAID) that's used to treat musculoskeletal inflammation and pain in horses.

During their careers, many high-level performance horses sustain injuries that require treatment with an effective antiinflammatory drug. Even minor inflammation and pain can translate into poor performance, shortened careers and vulnerability to more severe injuries.

Given these consequences, there are many medications used in performance horses — but there is only a short list of such medications permitted for use during Equine Canada-sanctioned competitions. Previously, that list has only included NSAIDs approved for use in Canada, and it didn't include firocoxib. The drug is approved in the United States where it's known by its brand names: Equioxx[®] for horses and Previcox[®] for dogs. Only Previcox[®] for dogs is approved in Canada.

Despite its lack of label approval in Canada, veterinarians have found that the canine-approved Previcox[®] was effective to treat minor pain in horses. While there are several other NSAIDs on the market, veterinarians favour firocoxib in some cases because it has a good safety profile, it's cost-effective and easy to administer by horse owners.

In most cases, this extra-label use of the drug isn't a problem. But at the elite performance horse level, such as at Equine Canadasanctioned events, testing positive for firocoxib resulted in disqualification from the competition and major fines for those responsible for the horse.

With a "zero tolerance" for firocoxib, the detection of any amount of drug in a blood or urine sample from a horse resulted in a violation, explains Dr. Trisha Dowling, a veterinary pharmacologist and professor at the WCVM.

"And as firocoxib is only slowly eliminated from a treated horse in its urine, horses can test "positive" for weeks after discontinuing the treatment," adds Dowling.

Variations in drug rules between the United States (where firocoxib is permitted by the U.S. Equestrian Federation) and Canada could even be deterring people from participating in Canadian events.

"I know a number of people who just choose to show in the States," says Dr. Mary Bell, an experienced competitor,



The author's own horse Lyric was part of the study. Lyric is attached to a urine collection device that allowed the researchers to study Previcox (firocoxib) elimination in equine plasma and urine.

veterinarian and former chair of the Equine Canada medication control committee.

"At one time, there were a number of NSAIDs licensed for horses in Canada. Piece by piece they just went off the Canadian market."

Bell says Equine Canada's decision to consider the off-label use of a licensed product such as Previcox[®] was stimulated, in part, because of a series of "drug positives" that resulted from a contaminant present in a compounded oral NSAID that is no longer available as a licensed product in an oral form.

With no hope of label approval on the horizon, the only option for Equine Canada regarding firocoxib was to make a rule variation allowing the extra-label use of the canine Previcox[®] tablets.

"In order to make an exception, what we really needed was the opportunity to have some quantification, some measurement of the urine and plasma concentrations in horses treated with normal doses," says Bell.

During the summer of 2015, Dowling and veterinary student Jessica Semper conducted a depletion study to determine the concentration of firocoxib in equine urine and plasma after a typical treatment regimen. The project's data would enable Equine Canada to make an informed decision and to set limits for firocoxib's use in performance horses. The WCVM study was supported by a grant from Equine Canada's Equine Medication Control Committee.

The WCVM research team treated 10 light horse mares with one 57-milligram Previcox[®] tablet per horse each day. After 14 days of treatment (the length of treatment recommended on the drug's U.S. label for horses), researchers regularly collected blood and

urine samples from the horses over a 24-hour period.

The samples were sent to Maxxam Analytics, Equine Canada's approved drug laboratory, for analysis. Once the WCVM team members completed their interpretation of the resulting drug analysis, Dowling made her recommendation to Equine Canada, which resulted in the rule change permitting the use of firocoxib during Equine Canada-sanctioned competitions.

If firocoxib is administered to horses in excessive doses, violations may be called for exceeding the study-generated threshold concentrations for blood and urine.

Equine Canada's decision to allow the appropriate extra-label use of the canine Previcox[®] tablets may help to alleviate the frustration that riders, trainers and owners experience when competing in Canada.

Bell says if a licensed firocoxib product for horses eventually becomes available, off-label use of Previcox[®] will be no longer be approved by the national organization.

"However, the detection times provided through this study will continue to be very applicable."

Jessica Semper of Nanaimo, B.C., is a third-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2015. Jessica's story is part of a series of stories written by WCVM summer research students.



Jessica Semper with one of the horses involved in the firocoxib study. Submitted Photo

Dairy study could help unite industry players

There is a hint of colour in the eastern sky as I run to the van parked on the curb. Just as I did in my childhood, I'm heading to the dairy farm to work.

November 19th, 2015 | By Rochelle Braun

However, instead of running across the pasture to feed our calves, I'm driving out to a farm as a researcher on Canada's first nationwide dairy study project, a Canadian version of the United States National Animal Health Monitoring Studies (NAHMS).

While our southern neighbors have been conducting national dairy studies for years, 2015 is the first year that Canada is performing similar monitoring research, which will provide researchers with uniquely Canadian information.

"For Canada, often when we refer to certain ... management practices that might affect disease [presence], we have to refer to the studies performed in the States," says Dr. Fabienne Uehlinger, a board-certified large animal medicine specialist at the Western College of Veterinary Medicine (WCVM) who is part of the national project.

The study will allow Canadian dairy farmers to be compared to a more accurate baseline, one based on data from their own country and their dairy industry system.

"The data that we will get from this study will help us with finding solutions to some of the big problems that are currently battling the dairy industry," says Uehlinger.

As a summer research student, I'm collecting information that will be used to determine welfare issues in Canada's dairy industry. I'm also collecting a variety of samples to determine the presence of zoonotic pathogens – illness-causing bacteria, for example, which humans can get from animals – and antimicrobial-resistant bacteria.

For the welfare evaluation, cows are graded on their cleanliness and their body condition. For example, we check to see if the cows are unacceptably thin and whether they have rub sores on their hocks, an area prone to rubbing if not enough bedding material is used. We also observe the cows to check for limps indicating pain.

In addition to collecting data for welfare and antimicrobial resistance, I'm gathering information about milking procedures that are important for several reasons. One key point is that improper milking procedure practices greatly increase the spread of disease from one cow to another.

I'm also reviewing biosecurity measures — a means to prevent disease from entering a farm, as well as to prevent illness from spreading from one animal to another within a farm. For example, on-farm biosecurity practices include restricting visitors to certain areas because they may unsuspectingly bring disease-causing organisms to the cows, and milking sick cows last so there's less chance of spreading disease to the healthy cows.

As part of the study we're collecting manure samples that will be analyzed for Johne's disease, caused by the bacteria



The author at work on a dairy farm.



Researchers evaluated milking procedures on farms.

Mycobacterium avium paratuberculosis. This disease causes loss of substances from the cow's blood. It also prevents cows from absorbing the normal amount of nutrients and water from their feed, leading to diarrhea and weight loss — and eventually death.

One southern Saskatchewan farmer told me he knew his farm tested positive for Johne's disease, so he must have brought it into his herd with a cow purchase. He's interested in getting the results back from our testing to see if the management practices he has implemented on his farm are working to decrease the presence of the disease in his herd.

We're investigating the presence of parasitic worms in the farms' dairy cows, which can result in fewer nutrients being absorbed by the cow. We're also taking blood samples to evaluate management effectiveness in the feeding of newborn calves on dairy farms.

As one farmer mentioned to me while I was collecting samples, most dairy farmers are individually minded and tend to focus on their individual farms and practices versus focusing on the national herd.

Not only will this study be a means of collecting vital data, it will encourage Canadian dairy farmers to think more as a community.

"[This study] will help to give farmers across the country a sense of how they are doing as an industry, and help them tackle issues of national concern," says Uehlinger.

Rochelle Braun of Landmark, Man., is a third-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2015. Rochelle's story is part of a series of stories written by WCVM summer research students.

Sable Island horses buck bacteria trend

Could bacteria resistant to antimicrobial drugs routinely used in both human and veterinary medicine be found in wild horses on a remote island in the Atlantic Ocean?

January 12th, 2016 | By Mary Timonin

By answering this question, Dr. Joe Rubin and members of his research team at the Western College of Veterinary Medicine (WCVM) hope to gain a better understanding of how bacteria carrying acquired resistance genes are passed between humans, domestic animals and wildlife species.

Their research has two major players: the horses living on Sable Island and the "bugs" — specifically *Escherichia coli* (E. coli) that these horses carry in their guts.

Sable Island, located 160 kilometres off Canada's Atlantic coast, is home to a population of over 500 feral horses – one of only a handful of wild horse populations in the world. The herd is descended from horses brought to the island in the late 1700s and has been protected by law from human interference since the 1960s.

These horses provide unique opportunities for researchers to study horse behaviour and health, as well as broader questions in ecology and evolution. They also represent a baseline population to study acquired antimicrobial resistance.

Rubin, an assistant professor in the WCVM's Department of Veterinary Microbiology, recognized the potential of the Sable Island horses to answer questions about how drug resistance spreads between bacteria as well as between animals.

The horses' isolated geographic location, their limited exposure to other species (including humans) and a complete lack of antibiotic exposure in the history of the herd are all factors that make this horse population so unique.

"The pressure for antimicrobial resistance and the potential exposure to resistant organisms from other animal species is quite limited," says Rubin.

Looking for acquired resistance in bacteria cultured from wildlife isn't a new concept, but the majority of studies have focused on birds or other species that interact with humans or agricultural production – increasing the potential for exposure to antimicrobial drugs or resistant bacteria.

Researchers frequently use E. coli in these surveillance studies for several reasons: it's found in the guts of most animals, it's easy to grow and it has many standardized tests established for its identification. E. coli also has the ability to accept and pass on resistance genes located on small pieces of DNA called plasmids that can be transferred between bacteria. Drug-resistant E. coli have been successfully cultured from a variety of wildlife species, and wildlife populations act as a reservoir for these resistance genes.



To determine if the Sable Island horses are acting as a reservoir for E. coli-carrying drug resistance genes, Rubin and his team used fecal samples collected from members of the equine herd. The collected samples are part of a multi-disciplinary Sable Island horse "gut biome" research project involving researchers from the University of Saskatchewan as well as other universities in Canada and abroad.

Researchers attempted to grow E. coli from each of these fecal samples. Next they tried to kill the bugs with a broad range of antimicrobial agents used in human and veterinary medicine. By keeping track of which antimicrobial drugs were effective in killing off the bugs and which were less effective, the scientists could develop a susceptibility profile for each isolated E. coli sample.

The WCVM researchers also have the ability to link back each E. coli sample grown in the study to the individual horse from which it was originally isolated. Researchers have been collecting census-level data on these horses since 2008, including family relationships between horses, geographic location on the island where the horses live and the social group they associate with.

"We actually know something about every single animal on the island," says Rubin.

This astounding depth and breadth of ecological data provides researchers with a unique opportunity to study the spread of bacteria carrying acquired resistance genes within an animal population. It also allows researchers to address questions such as whether bugs are shared within a family group, or the role of the environmental niche occupied by horses on the island.

Do the Sable Island horses represent a wildlife reservoir for resistance genes?

The simple answer appears to be no. Of the 500-plus fecal samples processed by Rubin and his research team, only a handful showed growth of E. coli at all — and those E. coli were "wimpy." In other words, the bacteria were unable to grow when exposed to even low concentrations of antimicrobial drugs.

For Rubin, the remarkably low levels of E. coli colonization (found in less than 30 per cent of the horse population) was one of the study's most surprising results — and it's one that he intends to pursue with more detailed analyses.

So far, it seems the same factors that make the Sable Island horses a unique microbiological benchmark population have been effective in protecting these horses from drug-resistant bacteria. But for how long? As more people visit Sable Island — Canada's newest national park reserve — and the number of drug-resistant bacteria present in migratory animals such as seals and wild birds rises, antimicrobial-resistant bacteria may soon become another part of the horses' remote world.

This study is supported by the Heather Ryan and L. David Dubé Veterinary Health and Research Fund.

Mary Timonin of Winnipeg, Man., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2015. Mary's story is part of a series of stories written by WCVM summer research students

Team explores radical therapy for Cushing's

This summer, Juliane Deubner gave her horse Tina a major "hair cut" so the 21-year-old fjord mare could beat the heat.

September 16th, 2014 | By Rebecca McOnie

Tina's coat clip isn't just for looks, it's out of necessity. The senior horse grows an excessive coat that is a prominent sign of the disease she has been diagnosed with: equine Cushing's disease.

Abnormal hair growth, laminitis and a change to fat deposit patterns (including a "cresty" neck) are signs of Cushing's disease. It's the most prevalent endocrine dysfunction among horses and is often diagnosed in horses older than 18 years.

Cushing's disease in horses, also known as equine pituitary pars intermedia dysfunction (PPID), is caused by excessive hormone secretion from a tumour in the brain's pituitary gland.

The pituitary gland, a small tear-drop shaped, disc-like protrusion from the base of the brain, sits below the hypothalamus, part of the brain responsible for hormone regulation. The pituitary gland's primary function is to produce and release hormones into the circulatory system.

Pituitary hormone production is normally regulated by chemicals, such as dopamine, from the hypothalamus. In PPIDaffected horses, neurons of the hypothalamus degenerate. As a result, the hypothalamus releases less dopamine for regulation of the pituitary gland. A tumour develops and hormone production in the pituitary gland increases when the concentration of dopamine is low.

Deubner, who lives on an acreage south of Saskatoon, Sask., recognized the signs of Cushing's disease in her mare almost three years ago. She was particularly concerned about Tina's bout of laminitis: "That's when it [PPID] gets serious."

Since then, Deubner has managed Tina's condition with daily doses of pergolide – the only drug treatment available for the disease. Pergolide imitates dopamine, acting as its replacement and decreasing the clinical signs of disease.

Despite the daily administration and price tag associated with pergolide, Deubner endorses the treatment. "If it keeps my horse useful, then it is worth the cost."

In fact, since her diagnosis, Tina has extended her riding career and is used as a school horse at a local stable.

More horses are living longer lives, thanks to appropriate preventive medicine and regular health management by their owners who care for their retired horses as pets. This has contributed to the prominence of PPID cases among the world's equine population.

"[It's] a chronic, incurable disease of the aging horse that is relatively common," says Dr. James Carmalt, a large animal surgeon and researcher at the Western College of Veterinary Medicine (WCVM).



Juliane Deubner with Tina – her 21-year-old fjord mare that has been diagnosed with equine Cushing's disease.

Carmalt is proposing a drastic shift in veterinarians' approach to treating equine PPID. The end goal of his research is to develop a surgical cure for the disease that will improve on the current standard of treatment.

As Carmalt points out, when humans or dogs suffer from pituitary-dependent Cushing's disease, the gold standard for care is surgery.

"Why not [surgery for] the horse?"

Surgical destruction of equine pituitary tumours could provide a long-term cure for PPID and eliminate the need for daily drug therapy.

Before performing a surgical approach, Carmalt's focus is on examining biomarkers of PPID, measurable indicators of the severity or presence of the disease. Association of a reliable chemical pattern with PPID may permit veterinarians to conduct more accurate and predictive testing for the disease. Particularly, the aim is to identify horses that are developing PPID but show no distinctive disease signs.

Carmalt reinforces that the PPID diagnosis and treatment are difficult for the veterinarian and the horse owner.

"The common veterinary problem of questioning the diagnostic tests, agonizing over whether to treat and then finally having someone treat the horse every day for the rest of its life has to become something of the past."

Current laboratory work on this project involves evaluating pituitary tissue samples for gene expression – measurements that may help to define the mechanistic effect of diminished dopamine regulation.

Another part of the research team's plan is to sequence genes of interest. This process could detect differences in hormone modification that exist between normal and PPID-affected horses. Carmalt's collaborator for this particular project is Dr. Suraj Unniappan of the Laboratory of Integrative Neuroendocrinology at the WCVM. The project has received financial assistance from the veterinary college's Equine Health Research Fund.

Early detection of PPID and a long-term cure for the disease may ultimately sustain a horse's career and allow horses to enjoy a longer, useful life, says Carmalt who acknowledges that his goals are ambitious.

"The status quo will remain as such unless someone somewhere makes a radical, paradigm shift in the thinking process surrounding this disease."

Back at Deubner's acreage, she continues to treat Tina for Cushing's disease. She used to give the compounded pergolide to Tina with a carrot or in her beet pulp, but her horse soon caught on and stopped eating any feed or treats containing the medication.

As an alternative, Deubner recently began using a tablet form of pergolide mesylate (Prascend®) to treat her horse.

"We dissolve the pill in water and squirt it into her mouth, that application seems to work the best," says Deubner, who thinks her horse's general well being has improved with the change in treatment.

"Her coat looks better, and she has a generally 'younger' look. [It's] something that I notice as a forever owner of this horse."

For Deubner, the enduring company of her affectionate fjord mare makes the management of PPID worthwhile.

Rebecca McOnie of Armstrong, B.C. is a second-year veterinary student who was the 2014 Equine Health Research Fund's undergraduate summer research student and was one of this year's Merial Veterinary Scholars. Rebecca's story is part of a series of articles written by WCVM summer research students.



Juliane Deubner with Tina – her 21-year-old fjord mare that has been diagnosed with equine Cushing's disease.



Rebecca McOnie, a veterinary student at the WCVM shows a horse brain and the small size of the pituitary gland.

"Flea-finder" probes for plague in Grasslands

Endless skies, wild bison and real cowboys – all are a part of life in Grasslands National Park. My summer research has brought me to southwestern Saskatchewan, an area harbouring some of the only native prairie left in Canada — and potentially, plague.

October 21st, 2014 | By Lauren Beaulieu

Just like your own pet dog, black-tailed prairie dogs (Cynomys ludovicianus) can have fleas, too. These fleas have been known to carry the bacteria *Yersinia pestis* – the causal agent of plague. That's right – the same bacteria that caused the Black Death in Europe during the 14th century.

It sounds scary, but there's actually minimal risk to human health unless you have a habit of snuggling prairie dogs, especially the flea-infested sort. In Grasslands, only one confirmed case of plague in a prairie dog was recorded in 2010. Since then, Parks Canada veterinarian Dr. Todd Shury and his research students have been monitoring levels of plague-carrying fleas.

This is where I come on to the scene. Against the vast backdrop of the prairie grasslands, I scamper about the prairie dog colonies, manoeuvring my plumbing snake with a flannel "swab" down the burrow of each unsuspecting victim.

The cute, loveable, talkative prairie dogs remain unharmed. This process is akin to cleaning your ear with a Q-tip — except my prize is fleas, not earwax. Once I've captured my unlucky prisoners, I send them to the Public Health Agency of Canada's (PHAC) National Microbiology Laboratory in Winnipeg, Man. PHAC will then identify flea species and run tests to detect plague-causing bacteria.

Why is it so important to save the prairie dogs from impending Black Death? First of all, Grasslands hosts the only native blacktailed prairie dog population left in Canada and their conservation status is "special concern" under Canada's Species at Risk Act.

Tara Stephens, a wildlife population ecologist with the Calgary Zoo's Centre for Conservation and Research, has been studying the dynamics of prairie dog colonies in Grassland for eight years as part of the Husky Energy Endangered Species Program.

"Black-tailed prairie dogs are a keystone species because they create a unique mosaic of habitat across the landscape that increases the heterogeneity and biodiversity of Grasslands National Park," says Stephens.

These cute critters not only function as landscape engineers, homebuilders and alarm systems, but they're also an important source of food for the black-footed ferret (BFF) — an endangered species.

Ferrets also use abandoned prairie dog burrows as shelter, but they're not the only park patron that moves into vacant real



Black-tailed prairie dogs can carry fleas, which have been known to carry the bacteria Yersinia pestis – the causal agent of plague.

estate. Burrowing owls, another endangered species, also claim the custom-built prairie dog homes as their own. Besides these two obvious beneficiaries, there are many more species whose livelihoods are connected to prairie dogs.

Stephens' research contributes to the science behind conservation of the black-tailed prairie dogs as well as the efforts to reintroduce black-footed ferrets. As she points out, Grasslands will use science to make informed management decisions, and that's one contribution she can make to help conserve this unique prairie ecosystem.

Stephens thinks it's vital to keep monitoring and expanding the plague-focused research; "We really have little understanding of plague ecology in Canada." She refers to the devastation that plague has caused across the border in American prairie dog colonies. "There's a spectrum of what enzootic and epizootic levels [of plague] can look like. It might take five or more years to catch a signal of plague in the system, especially if it's at enzootic levels."

Plague can be hard to find if it's not present at high levels, but this doesn't mean it's not doing any damage. To boost my chances of finding evidence of plague, I have been taking blood samples from dogs (pet dogs, not prairie dogs). Dogs will mount a sizeable immune response when infected with plague-causing bacteria but usually go on to lead healthy lives. Antibodies from the immune response remain in the dogs' blood, providing a marker to use in plague monitoring.

Plague in GNP has been elusive and this makes searching for it a bit tedious. Don't get me wrong, my job does have its perks. My commute to work is a peaceful hike, my office is the rare prairie grassland and my co-workers are chattering prairie dogs.

Stephens sums up the magical atmosphere in the southwestern park: "It feels so hidden, and I love that about Grasslands."

When it comes to being hidden, the plague is also doing a good job, which reminds me – I have to get back to finding fleas!

This research project is supported by the Western College of Veterinary Medicine's Interprovincial Undergraduate Student Summer Research Program, Parks Canada and the Calgary Zoo's Centre for Conservation and Research. Visit explore.org to see remote footage of the black-tailed prairie dog colonies.

Lauren Beaulieu of St. Paul, Alta., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2014. Lauren's story is part of a series of articles written by WCVM summer research students.



Juliane Deubner with Tina – her 21-year-old fjord mare that has been diagnosed with equine Cushing's disease.

Survey gives personal view of cattle farming

I'm driving through lush pasture on a Saskatchewan cow-calf farm, chatting with a producer about his beef cows that dot the green hillside. As we park, the animals wake from their mid-morning snooze and amble single file toward us – eager for treats and a scratch.

November 3rd, 2014 | By Ellen Watkiss

This is a side of cattle farming that I feel lucky to see.

With only two per cent of Canadians living on farms, few consumers truly know where their food comes from. Whether they get their information from a producer group's public relations campaign or from undercover footage of abusive practices on farms, the Canadian consumers' view of farming is often muddied by bias.

To address the ever-widening gap between producers and consumers, I'm skipping the middle man and directly asking beef farmers about their connection to their animals, their motivation to farm and the emotional investment they have in farming.

Dr. Joe Stookey, a professor at the Western College of Veterinary Medicine (WCVM), had a couple of reasons for starting this study.

"Within my social circle I'm friends with lots of beef producers, and when you talk to them, you can see their passion for their animals and for their work," says Stookey.

"As an industry, we often say that we care about our animals, and I believe that we do. But as a scientist, I want to be able to show people scientific evidence of it before we can tell that to the public."

As a veterinary student, the project is an opportunity for me to get to know farmers on a whole new level. My challenge is to bring that level of understanding to the public in a way that's as unbiased as possible.

The project is still in its pilot stage so the interview process is quite fluid. I'm interviewing eight farmers from around Saskatoon, and each interview is a little different. I'm trying to figure out what makes farmers tick – what makes them open up and show their emotion. I'm also asking them what they think are the most important issues facing farmers today.

What's interesting is how each farmer's background gives him or her a unique perspective on farming. For some producers, the bond with the individual animals is strong enough to bring tears to their eyes at the thought of losing them.

For others – such as a fifth-generation cattle farmer whose family homesteaded land over a century ago – the most important aspect is to uphold their family's heritage.

"For me, the most rewarding thing is not being the last [person in the family] to have cattle," says the producer. "I won't be the reason we have to sell or be done our [family's] consecutive streak of 125 years."



What drives other cattle producers is their passion for environmental stewardship, protection of prairie habitats and promotion of sustainable grazing practices.

"I just love what we're doing with the land – what's happening to it and how it's improving," one producer tells me. A common thread that runs through all of the interviews is the underlying pride these farmers have in their animals and their lifestyle.

Until the project moves beyond the pilot stage, we can only scratch the surface of how producers feel about farming and their cattle. But by using the results of this study, we hope to show that our interview process is a reliable means of gauging farmers' connection to their animals.

"A one-on-one interview allows for the opportunity to capture sentiments and quotes that are honest and heartfelt. And it allows us to capture spontaneous responses and comments that we had not anticipated," says Stookey.

"We're hoping to tap into the emotional connection and passion that producers and ranchers have for their cattle, and I think the best way to do this is to hear them talk openly about their operation and their cattle."

By expanding to a larger study, we can provide the public with valuable information about who Canadian beef producers are and what they get out of farming. And with a better understanding of the industry and of farmers themselves, the public can make more informed choices at the grocery store.

So next time you're driving past a field full of grazing cows or looking at packages of fresh steak and hamburger on a grocery shelf, remember that the person raising those animals and your food has much more invested in the business of farming than just money.

To them, cattle are a way of life, a source of pride and joy, and a means of survival.

Ellen Watkiss of Saskatoon, Sask., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2014. Ellen's story is part of a series of articles written by WCVM summer research students.

Study may offer therapy for heavey horses

Sucking air through a straw. Those are the words that many people with asthma use to describe their frightening struggle to breathe during an asthma attack.

November 12th, 2014 | By Hayley Kosolofski

Now imagine a 1,000-pound animal experiencing the same panic-stricken feeling.

For a horse, that's what it's like during an acute episode of recurrent airway obstruction (RAO) or heaves. This asthma-like condition is a chronic, inflammatory disease of the lungs that worsens when an affected horse is exposed to dust and mould. As the horse's airways narrow, it increases its breathing effort until it starts to cough.

This debilitating disease detracts from horses' quality of life and limits their career, and while RAO affects many horses in Western Canada, veterinarians still don't fully understand the problem.

"Like many veterinarians, I have struggled with understanding the disease process of RAO and treatment of severe cases," says Dr. Michelle Husulak, a resident in equine field service at the Western College of Veterinary Medicine (WCVM). She and her supervisor, Dr. Julia Montgomery, are conducting a study investigating treatment options for horses with RAO that will hopefully answer some questions about the disease process.

In human medicine, current research in asthma suggests bacteria may play a role in the disease in people. As well, horses with RAO often have bacteria in their lungs – but researchers still don't understand the importance of the bacteria in relation to the disease.

"Often we find bacteria that are not causing a pneumonia and may or may not be normal flora. In these cases we are unsure if treatment with antibiotics is required," explains Husulak.

She wants to determine if targeting these bacteria with antibiotics – on top of traditional therapy for heaves – helps the horses improve. Answering that question may also shed light on the role of bacteria in the disease process.

Traditional therapy for RAO consists of environment management – reducing exposure to dust and mould by keeping the horse outdoors on pasture, soaking hay or feeding hay cubes, and using a low-dust bedding such as wood chips.

As well, veterinarians often prescribe drug therapy: corticosteroids such as Dexacort[®] (dexamethasone) to reduce lung inflammation along with bronchodilators such as Ventipulmin[®] (clenbuterol) to open up the horse's airways.

Husulak wants to know if adding in antibiotic therapy will further help the horses improve from an acute episode of heaves.

"Do these horses need to be treated with antibiotics to help resolve their clinical symptoms or is treating with antibiotics considered inappropriate use of antibiotics?," says Husulak. "This is a question I would like to answer."



For her research, Husulak is recruiting horses with heaves in the Saskatoon area. Before the horses can be enrolled in the study, the diagnosis of RAO has to be confirmed and bacteria must be present in their trachea.

Once they're part of the study, Husulak and members of her research team give horses a thorough physical examination with special attention paid to the lungs. The clinicians use a technique called "rebreathing" where they place a plastic bag over the horse's muzzle for a few minutes so the animal rebreathes the air it expires. The horse will naturally breathe deeper and allow Husulak to hear more lung sounds with her stethoscope.

The research team also performs two tests – the tracheal wash and bronchoalveolar lavage – to retrieve samples from each horse's upper and lower airways.

Once the veterinarians can confirm an RAO diagnosis and bacteria are found in the trachea, they start the horses on a treatment protocol. They also ask owners to keep their horses outdoors as much as possible and to soak their hay. As well, all of the RAO-positive horses receive steroids and bronchodilators.

To determine if the antibiotic therapy is effective, half the horses receive antibiotics (the treatment group) while the other half receive saline (the control group). Neither Husulak nor the horse's owner knows whether the horse has received antibiotics or saline – ensuring that there isn't any bias when assessing the horse's improvement.

After the treatment course is finished, Husulak visits each horse a second time to re-perform the physical exam, tracheal wash and bronchoalveolar lavage and to assess its improvement.

How does she determine if the horses have improved?

"We are looking at the clinical signs such as respiratory rate and effort, nasal flaring, nasal discharge and lung sounds. We are also looking at the tracheal wash bacterial culture, and the inflammatory cells and proteins on bronchoalveolar lavage," says Husulak, who has tested two horses so far.

She and her colleagues will continue testing horses for the study over the next few months. And ultimately, if results of the WCVM project show that antibiotic therapy can help horses with RAO to recover from acute episodes of the disease, veterinarians would have something that could help their equine patients – as well as their clients – breathe easier.

Hayley Kosolofski of Sherwood Park, Alta., is a third-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2014. Hayley's story is part of a series of articles written by WCVM summer research students.



Dr. Husulak listens to lung sounds with her stethoscope in a horse with RAO.

Team uses calf hair cortisol to measure pain

Researchers at the University of Saskatchewan are investigating the issue of pain associated with castration in beef cattle and their research involves haircuts for calves.

March 13th, 2015 | By Travis Marfleet

Dr. John Campbell, a large animal professor at the Western College of Veterinary Medicine (WCVM), is leading the research team whose members are based at several U of S colleges.

Their focus is on the stress hormone cortisol as an assessment of pain and stress in beef calves following castration. While cortisol is typically measured in saliva or blood, the U of S team is measuring cortisol in hair samples collected from castrated or non-castrated calves.

Dr. David Janz, a professor in the WCVM's Department of Veterinary Biomedical Sciences and one of the study's coinvestigators, employs the technique primarily for studying wildlife species. Its main advantages: collecting hair samples is much easier than drawing blood samples, plus it minimizes stress on the animals.

Although hair analysis for drug and hormone compounds is relatively old hat in human medicine and toxicology, the technique hasn't been widely used in the North American beef industry.

"This project is really our first step to determining if it is a good objective measure of stress and we're able to do it in a sort of clinical trial approach," says Campbell.

He believes hair cortisol analysis will be an important research tool to assess pain and stress in several aspects of cow-calf and feedlot beef production in the future.

Castration is a commonplace practice in the beef industry that prevents undesirable breeding, improves meat quality and reduces aggression in male calves. Although it's widely accepted that all castration procedures involve some level of pain and discomfort for calves, producers are still without cost- and time-effective options for controlling pain when castrating large groups of calves.

Cattle producers are naturally hesitant to adopt new practices without sound scientific backing and economic sensibility. But as animal welfare concerns become more prominent, there's a growing need for pain management options whose effectiveness can be accurately measured.

For this particular study, researchers collected a hair sample from each calf on an area of the hip that was shaved down to the hide two weeks earlier when the calves were initially castrated. This approach gives a wider picture of cortisol production throughout the study period since new hair growth at the shaved patch is actively incorporating cortisol produced following castration.

The study's main goal is to assess the efficacy of a long-acting



calves that was involved in the WCVM's cortisol analysis study. Calves that was involved in the WCVM's cortisol analysis study.

anti-inflammatory drug (meloxicam), given at the time of castration, to manage post-procedure pain and inflammation in beef calves. If the drug is effective, there should be lower levels of hair cortisol in the castrated calves receiving the anti-inflammatory drug versus calves that only receive a saline injection after castration.

Cortisol serves an important role in maintaining energy levels and biological functions following exposure to stressors, disease or painful procedures. For animals, coping with these situations is a major energy drain since more fuel is needed to initiate wound healing, mount an immune response to infection, or maintain body condition when appetite decreases.

Veterinary student Ellen Watkiss shaves a spot on a calf's hip before castration. Two weeks later, researchers collected hair samples from the shaved areas on each of the study's calves to analyze stress.

The short-term benefits of cortisol production are offset if stressors or pain persists. Long-term production of the hormone can cause weight loss and poor immune function, potentially harmful effects that are of particular concern to the beef industry.

The study design accounted for important events, such as wound healing and post-procedure inflammation, that occurred after castration without additional animal handling. As well, all of the study calves wore automatic data recorders on their hind legs so researchers could track standing and lying times.

All of these measures mimic on-farm practices where cow-calf pairs would typically be sent out to pasture shortly after the calves were castrated and not repeatedly handled by producers.

"Research that accurately reflects on-farm practices is key to producing meaningful data that could influence beef production and future research areas," says Dr. Joseph Stookey, an animal behaviourist and animal welfare researcher who is part of the U of S research group.

The team tracked hair cortisol levels of individual calves throughout a typical cow-calf season. And although the current phase of the study focuses on castration, the research will expand to assess hair cortisol levels following other stressful events in the life of beef calves such as weaning and feedlot arrival.

The Saskatchewan Agriculture Development and the WCVM's Interprovincial Undergraduate Student Summer Research Program provided financial support for this research project.

Travis Marfleet of Maidstone, Sask., is a second-year veterinary student who was part of the WCVM's Undergraduate Summer Research and Leadership program in 2014. Travis' story is part of a series of articles written by WCVM summer research students.



Veterinary student Ellen Watkiss shaves a spot on a calf's hip before castration. Two weeks later, researchers collected hair samples from the shaved areas on each of the study's calves to analyze stress.

Poop, parasites and public health

It may look like ordinary, everyday dog poop, but to researchers at the Western College of Veterinary Medicine (WCVM), those little lumps contain a treasure trove of public health information.

February 3rd, 2014 | By Laura Davenport

That's one of the key facts that I learned last summer as a WCVM research student, travelling around Saskatchewan collecting dog feces — a job that gave me first-hand experience in veterinary public health.

I worked with Dr. Emily Jenkins and her PhD student, Janna Schurer, in the WCVM's Zoonotic Parasite Research Unit. Schurer is surveying populations of dogs in northern and Indigenous communities to determine the prevalence of parasites and the risk of transmission between dogs and people.

Schurer chose to focus on these communities because of three factors: they lack regular access to veterinary services, they have large free-roaming dog populations and many of their residents rely on harvested wildlife (country foods). Her study's preliminary results show that parasite prevalence levels in the communities' dogs are up to 20 times higher than those in dogs living in areas with easily accessible veterinary service — such as Saskatoon.

"Dogs are particularly interesting because they bridge the gap between veterinary and public health," says Schurer, adding that the species has potential as a sentinel surveillance system for human disease.

Jenkins and Schurer are especially interested in Echinococcus tapeworms that have been found in wild and domestic animals in Canada. When people accidentally ingest eggs from the environment (passed by an infected carnivore), they can develop into cysts in the lungs and liver — or in less common places such as the brain — sometimes with tragic consequences.

Echinococcus infection was once a relatively common occurrence in the North when sled dogs were used for transportation, but the incidence has significantly decreased. While infection with this parasite is now a rare phenomenon, surveillance, prevention and education will help to keep the risk low for people.

As well, recent cases in dogs in Canada have raised concerns that introduced strains of *E. multilocularis* may pose new threats to animal and human health.

Since Echinococcus eggs are a health hazard in people, the standard protocol in endemic areas of the world is to freeze fecal samples from carnivores at a temperature of -80 C for three days. This temperature renders the eggs non-viable and eliminates the risk of human infection.

But not all areas of the world have Echinococcus — opening the debate on the accuracy of detecting other parasite species that have lower tolerance to extreme cold. Parasite egg counts could be significantly decreased in frozen samples if the eggs are damaged beyond recognition.

Part of my summer project explored the effects of freezing protocols on parasite egg counts in fecal samples from

horses and dogs. I found that hookworm and trichostrongyle roundworm eggs change their appearance significantly — and some are not recognizable. This means that fecal flotations may be underestimating egg counts of some parasites if samples are frozen before processing.

However, our work showed that parasite prevalence was relatively unaffected by freezing which is good news for our surveys.

In addition to trolling the microscope for parasite eggs, I travelled with Schurer and Jenkins to remote and Indigenous communities in Saskatchewan where we collaborated with community organizations including the Canine Action Project and Team North.

Key objectives of these initiatives are to develop and implement humane and sustainable animal population control. Another goal is to increase basic veterinary services by organizing preventive health clinics that include vaccination, deworming and surgical sterilization. We worked in co-operation with the communities on the planning and funding of these events.

To help increase community awareness of veterinary services and to enhance the educational component of these community-based clinics, we created posters about parasites and prevention in their pets that can be posted in schools and public meeting areas.

These clinics gave me the chance to hone my skills in physical examinations, surgical preparation and monitoring, and surgical skills. I also collected blood samples from more than 100 dogs that were tested for exposure to vector-borne diseases such as heartworm and Lyme disease. Fortunately, we didn't detect these diseases in these dog populations.

Our group was also involved in the University of Saskatchewan's SCI-FI VetMed summer day camps at the WCVM. I helped out in labs where the campers ran fecal flotation tests and examined the results for eggs. They also had the chance to explore many other weird and wonderful parasites. I couldn't believe how excited the campers were to play with poop!

My summer research job highlighted the integral role of veterinarians in public health. It gave me a new appreciation for the creepy, crawly creatures we can't see with the naked eye, and it taught me many valuable veterinary skills. I plan to remain involved in public health and animal welfare projects, and I'm excited to continue exploring the career options in veterinary medicine.

Funding for my research project was provided by Zoetis Canada and Idexx Laboratories.

Laura Davenport of Saskatoon, Sask., is a second-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013. Laura thanks the entire Zoonotic Parasite Research Unit for "taking me under your wing and giving me such a great summer experience."

Nesfatin-1: obesity, diabetes fighter?

In North America, metabolic diseases such as diabetes and obesity are becoming epidemic among people as well as their pets.

February 13th, 2014 | By Laura Davenport

As many as 50 per cent of cats and dogs in domestic households are overweight or obese and science still doesn't fully understand why some individuals are more prone to metabolic disease than others.

Dr. Suraj Unniappan, an associate professor in the Western College of Veterinary Medicine's (WCVM) Department of Veterinary Biomedical Sciences, is helping to shed some light on the subject. The researcher is now focusing to better understand the function of a relatively less studied novel protein, nesfatin-1, that was discovered in Japan in 2006.

Nesfatin-1 suppresses appetite to make people and animals feel full after a meal. It also stimulates insulin release so that glucose moves from the blood into the cells, thus helping to maintain energy balance. When nesfatin-1 was administered to rats, they not only ate less but used more fat as an energy source and became more active.

Nesfatin-1 is produced throughout the body but has been found to be abundant in the hypothalamus (a region of the brain that regulates feeding and body weight) as well as the fundic region of the stomach and the insulin-producing pancreatic islet beta cells. It's also found circulating in the blood.

So far, researchers have mainly studied nesfatin-1 in humans, rodents and fish. These studies have shown it's an important molecule that's naturally occurring and multi-functional in these species. But other than a couple of recent studies involving pigs and dogs, nesfatin-1 in domestic animals still remains poorly understood.

For my summer research project, I attempted to gain a comprehensive understanding of nesfatin-1 in domestic animals by investigating its expression in the stomach, pancreas and blood of animals including cats, dogs, pigs, horses, cows, sheep, bison, chickens and rainbow trout. The tissue samples were provided by a large number of researchers at the WCVM and the University of Saskatchewan.

Proteins are often studied by using antibodies that are tagged in some way so you can visualize them. For this study, I looked at nesfatin-1 in tissue samples by incubating it with a fluorescentlylabelled antibody so it could be viewed under a fluorescence microscope. I also used antibodies to detect it circulating in the blood, but this test uses a colour change reaction to visualize the results.

Using scientific databases, I also collected the sequences for nesfatin-1 from over 100 species of animals and compared them using computer software programs. As it turns out, nesfatin-1 is highly conserved among species. In other words, the sequences are nearly identical in vertebrates and highly similar in some invertebrates. This evolutionarily conserved structure of the protein suggests similar functions for the nesfatin-1 across species. We expected to find the nesfatin-1 protein in all of our species of interest, especially since it is so highly conserved. What we actually found was that it appeared in the blood of all of our study's target species as well as in their stomach and pancreas.

There was one exception: we didn't find nesfatin-1 in the pancreatic islets of cats as we had expected. This is an interesting finding — especially since cats are more prone to metabolic disease. More work needs to be done to understand why they are different than other species.

My research findings are important as it is the first set of information on nesfatin-1 in a large number of domestic animals and provides direction for future studies.

Scientists including Unniappan are exploring the anti-obesity and anti-diabetic potential of nesfatin-1. Since it's a natural protein that the body makes itself, it would have fewer side effects than compounds that are not. But much more work needs to be done to understand how nesfatin-1 produces its effect in the body and what other functions — some potentially adverse — it may have.

Research in Unniappan's lab is funded by grants from the Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council (NSERC) of Canada, Canada Foundation for Innovation (CFI) and the Saskatchewan Health Research Foundation (SHRF). My research was funded by the U of S and the WCVM.

Katie Morton of Quesnel, B.C., is a second-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013.

Software simplifies cardiovascular analysis

Research has shown that the way your blood flows through your arteries may be more effective at predicting your risk of dying from cardiovascular disease than using the blood pressure cuff at your doctor's office.

February 28th, 2014 | By Kaylee Bohaychuk

At each heartbeat, blood pressure and flow travel in waves down the length of your arteries, just like a pebble cast into a pond creates ripples on the water's surface. The relationship between the blood pressure and flow waves generates biological markers for arterial stiffness that appear to be important in predicting cardiovascular mortality.

Arterial stiffness is important because it's closely related to heart function and vascular health as well as to small vessel disease of the kidney and brain — conditions that lead to kidney failure and dementia.

Since this study's results were published, many human clinical researchers have been taking a closer look at blood pressure and flow waves to determine arterial stiffness. However, basic and veterinary scientists have yet to catch up to the advances made by their human clinical counterparts.

This knowledge gap is partially due to the mathematical background needed to understand the relationships between blood pressure and flow waves and the availability of practical software needed to perform the analysis.

WCVM student Kaylee Bohaychuk (left) and postdoctoral fellow Mirhosseini Naghmeh.

This is where I step in. I plan to bring blood pressure and flow wave analysis to the cardiovascular toxicology lab in the Western College of Veterinary Medicine (WCVM) with my supervisor, Dr. Lynn Weber, and postdoctoral fellow Dr. Naghmeh Mirhosseini.

I'm developing a software suite that will allow us to examine the effects of cardiovascular toxins on cardiac function and vascular rigidity in greater detail. My software will be available at no cost to other researchers so they may also take advantage of the information that the blood pressure and flow waves tell us about arterial stiffness.

WCVM researchers in the cardiovascular toxicology lab are investigating the effects of vitamin D deficiency versus toxicity on the cardiovascular system. The goal is to find a safe range of dosage for vitamin D supplementation.

"Vitamin D deficiency can cause hypertension, arteriosclerosis, myocardial infarction and even a sudden heart attack," says Mirhosseini, adding that people need to take vitamin D supplements in an appropriate dosage.

However, very few studies show the potentially negative effect of high doses of vitamin D on the cardiovascular system. What's concerning is that for people suffering from severe vitamin D deficiency, Mirhosseini says the recommended dosage is much higher, but no one is certain about its safety. My section of the project is looking at arterial stiffness caused from inappropriate vitamin D supplementation.

I began working on the vitamin D project during the summer of 2012 with the Merial Veterinary Scholars program. I had just completed my first year of veterinary medicine at the WCVM, and I was eager to show that my previous background in computing science was extremely applicable to veterinary biomedical science.

In 2012, I had an idea about how we could measure the stiffness of an artery from the pressure wave — but it wasn't possible to calculate using the commercial software in our lab.

Instead, I whipped out my laptop and began programming. The result was PWanalyze — software that calculates metrics of arterial stiffness based on pressure waves recorded in arteries.

Last summer, I returned to the WCVM lab with funding from the college's Interprovincial Summer Research program. Spurred on by the success of my first summer, I've been delving deeper into the mechanics of arterial stiffness. My plan is to release a second software suite that focuses on pressure and flow waves by the beginning of this summer.

Ultimately, I hope to make the cardiovascular analysis possible for laboratory species. There are many studies on humans that use this technique, but ironically, there are very few studies on laboratory species that are used to model cardiovascular disease.

This is one example where the basic science research in animal models hasn't preceded the clinical use of the technique in humans.

Kaylee Bohaychuk of Ardrossan, Alta., is a third-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013. Kaylee is also working toward her Master of Science degree in veterinary biomedical sciences.

What makes a good egg?

As a woman who is over 30 and childless, I can identify with other females my age who are in that inevitable countdown toward 40 and trying to decide whether we should have children before our fertility declines.

April 16th, 2014 | By Serena Caunce

Some women consider freezing their eggs while they are still young — but how do we know what makes a good egg versus a bad one?

I learned more about this topic as a summer research student in Dr. Jaswant Singh's research lab at the Western College of Veterinary Medicine (WCVM). Singh and his research team have been using assisted reproductive techniques in cattle as a model for human reproduction to determine what characteristics make a good quality egg.

Characteristics of a good quality egg include oocyte competence — the ability of the oocyte (the egg) to be fertilized and develop into an embryo.

Each oocyte grows within a follicle in the ovary and microscopic changes occur in an oocyte that are related to this environment. Follicles are stimulated to grow under the influence of follicle stimulating hormone (FSH). Before ovulation, there is an increase in luteinizing hormone (LH), a hormone that an oocyte needs to continue its development before fertilization.

If the levels of LH and estrogen are appropriate the follicle will release the oocyte, while in the absence of these hormones the follicle regresses and ovulation does not occur.

We used these ideas in a superstimulation protocol to cause many follicles to grow to a dominant size so we could have several oocytes to work with. Superstimulation is done by injecting FSH to higher than normal levels to have more preovulatory follicles.

Serena Caunce of Calgary, Alta., is a second-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013. Serena's story is part of a series of articles written by WCVM summer research students.

Our current project is building on that of Dr. Fernanda Dias' work for her PhD program that she recently completed in the WCVM's Department of Veterinary Biomedical Sciences. Dias was conducting research to determine the effects of follicular aging on granulosa cells in follicles of cattle after superstimulation.

She compared a conventional, four-day superstimulation protocol of FSH injections with a seven-day protocol of FSH injections and discovered that many more follicles reached dominant size using the longer treatment.

Additionally, she had another group of cattle that only received



four days of FSH, but underwent a withdrawal period prior to injection of LH to initiate maturation of the oocytes.

What Dias found was these oocytes were not as competent as the oocytes that matured in the seven-day FSH injection group. In other words, the FSH withdrawal prevented the oocytes from developing into embryos.

Previous research investigations conducted by Singh and his team have shown that women after 35 years old and cows in their early teens share similarities in follicular development, reproductive hormone levels, embryo development and oocyte quality.

"There are some things that are specific, but in general, they follow the same principles," says Dias. "We use the bovine as a model for aging. A lot of projects use bovine or other species as a model."

In the current study, we used a similar superstimulation protocol then using a fluorescent marker that is converted by reactive oxygen species (ROS) which we can visualize on a confocal microscope.

"Oxidative stress is when the cell is not going through the process right, not completing the whole process of respiration. When this happens, they start to produce ROS... and that's toxic for the cell," says Dias. "Evaluating how much ROS we have in the cell will show how healthy that cell is."

The cell has its own ability to produce glutathione, an enzyme that will remove ROS. Evaluating the amount of glutathione is a future endpoint of the project.

"If you have a lot of ROS build-up in the cell, the cell will try to produce glutathione as much as it can. If it cannot cope, then the cell will go through apoptosis and die," says Dias.

Now that Dias has completed her graduate program at the WCVM, she is working as a lab director at an in vitro fertilization

clinic — Saskatoon's Aurora Reproductive Care — that assists women who are having infertility problems.

While "physiology is physiology," the jump from reproductive science in animals to that in humans will still be quite a change for the scientist: "I think the biggest challenge that I will face is working with women who have problems with fertility. Right now we have cows that . . . don't have any problems with their fertility. So going to work with women that have fertility problems I think will be a challenge."

While I still have time to decide whether I need to visit Dr. Dias at the fertility clinic to determine if my eggs are competent, I believe that it's important for women my age to be informed about this concept.

Serena Caunce of Calgary, Alta., is a second-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013.

WCVM scientists focus on moon blindness

Six years ago, Shelley and Ray Ruiters purchased an Appaloosa mare named Annie from friends who thought she would be a great fit for the couple.

December 7th, 2013 | By Laura Field

It turned out that the Ruiters' friends were exactly right. "From the first day I met her we just rode off on our own and she never missed a beat," says Shelley.

About a year after Annie arrived at the Ruiters acreage near Saskatoon, Sask., her owners noticed tearing and squinting in her right eye. Soon after, the mare was diagnosed with equine recurrent uveitis (ERU) or moon blindness.

"I had absolutely no knowledge of this disease nor did any of my riding friends prior to Annie's diagnosis," says Shelly.

The Ruiters' mare was suffering from one of the oldest known equine diseases and the leading cause of blindness in horses. Uveitis is swelling of the choroid, the area that supplies blood to the eye. ERU is characterized by chronic bouts of inflammation in the eye that causes ongoing damage — eventually leading to blindness.

Clinical signs of ERU include tearing, squinting and sensitivity to light. Veterinarians might notice lower pressures of fluid in the eye, an iris that is adhered to the lens, and small cataracts.

Annie's struggle with the eye disease coincided with Shelley's own diagnosis of breast cancer.

"Riding (Annie) settled my mind and prepared me for what was to come. Annie carried me safely two weeks after my surgery," says Shelley, who derived strength from her horse.

"Anyone who has ever breathed into their horse's nostril knows that nothing beats the smell of a horse when you are a little down."

Shelley's cancer is now in remission, but in May 2013, Annie developed a painful ulcer on her remaining eye that wouldn't heal. The Ruiters had to make a difficult decision.

"On our last ride together, it was apparent that Annie had lost her confidence. Her vision was impaired, and she struggled to keep both of us safe," says Shelley, whose beloved 12-year-old mare was euthanized this spring.

"I just couldn't stand to see her suffer any more. I lost an amazing animal friend in the prime of her life who had no other existing medical concerns."

Diagnosing ERU can be challenging, says Dr. Lynne Sandmeyer, a veterinary ophthalmologist at the Western College of Veterinary Medicine (WCVM). Before a diagnosis can be confirmed, clinicians must rule out other causes of uveitis including parasites, viruses, trauma or a rupture of the lens.

"The sad thing about it is that it can often be missed so that the animal can be going blind without anybody noticing," says Sandmeyer.

There is no cure for ERU, and treatment focuses on minimizing inflammation in the eye. Lifelong treatments include anti-

inflammatory drugs that are given as eye drops or orally to the horse. Another constant medication is atropine that causes pupil dilation. Dilating the pupil eliminates painful muscle spasms in the eye and prevents the iris from sticking to the lens.

"The downsides to continuous treatment are the need to treat the horse several times a day with topical medications as well as chronic use of oral anti-inflammatory drugs which can lead to gastrointestinal irritation, especially in performance horses," says Sandmeyer. She is part of a long-term study of ERU along with her colleague, Dr. Bianca Bauer.

This year, the research team is gathering a history of ERU at the WCVM's Veterinary Medical Centre by going through medical records in search of all suspected cases of ERU in the past 10 years.

Researchers are gleaning valuable information from the patients' records such as the breeds and sex most affected by ERU, descriptions of disease progression, length of time before a confirmed diagnosis, and the time from diagnosis to euthanasia or eye removal surgery.

Appaloosas such as Annie are of special interest to the research team. In a study conducted over eight years (1987 to 1995), ERU-affected horses were tested and Appaloosas showed a 25 per cent prevalence for the disease. In comparison, other horse breeds only had a 10 per cent prevalence for ERU.

Sandmeyer and her colleagues recently discovered a gene known as "LP" (Leopard complex) that causes the Appaloosa to have the spotted coat patterns. They uncovered an association between horses having two copies of the LP gene and a disease in Appaloosa horses called congenital stationary night blindness (CSNB).

The WCVM researchers are now interested in determining whether there is a link between the LP gene and Appaloosa susceptibility to ERU.

The Ruiters are among the many horse owners who will be anxious to learn about the WCVM team's findings after watching their own horse suffer from the devastating disease. ERU's cause has yet to be discovered, and the WCVM research team's first steps into studying the genetic component of ERU are critical if horses like Annie are to be saved in the future.

"The care of an animal with this condition can be exhausting and costly," says Shelley. "We did it all because Annie was loved and appreciated."

Laura Field of Holbein, Sask., is a fourth-year veterinary student who participated in the WCVM's Undergraduate Summer Research and Leadership program in 2013.

A safer solution for a sticky problem?

When my little dog Maggie was young, she would chew anything she could get her paws on: a lamp cord, cell phone charger, TV cable, garbage cans, clothing, the bathroom curtain and even the bottom of a door.

June 1st, 2013 | By Melissa Cavanagh

But most of all, she loved to gnaw on the pig's hoof that I gave her to chew.

One day Maggie seemed "off." After a series of X-rays, our local veterinarian discovered that a chunk of pig's hoof was sitting somewhere in my miniature Australian shepherd's small intestine.

Maggie's story has a happy ending — the piece of hoof passed through her without surgery. But other chew-happy dogs aren't so lucky: sometimes, swallowed objects can actually get stuck inside them.

One common "sticking spot" where foreign objects can become lodged is the esophagus right in front of a dog's heart.

"Usually that specific spot is more commonly a problem with smaller dogs just because of the way their anatomy goes," says Dr. Amanda Tallant, a surgical resident at the Western College of Veterinary Medicine (WCVM). "Bigger dogs usually get obstructions at different places."

Most esophageal blockages are treated with endoscopy: veterinarians insert a tiny instrument into the dog's esophagus and use it to push the foreign object into its stomach.

But if the object has been stuck there for a while, it may damage the dog's esophagus. "The covering of the inside of the esophagus can be ulcerated through by having something sit there," explains Tallant.

She adds that a dog with a foreign object stuck in its esophagus will often regurgitate food (bring food back up shortly after eating) — a common symptom of esophageal obstruction. But if owners mistakenly think their dog is vomiting, they may not take their dog to the veterinarian right away.

"Surgery is actually not the ideal option at all, but in bad cases that have been sitting there for a while, you have to do surgery because the esophagus isn't intact."

Right now, small animal surgeons have a choice of two surgical approaches to remove an obstruction from a dog's esophagus. They can perform a median sternotomy (splitting of the breastbone) or they can enter the dog's chest cavity through the space between a dog's fourth and fifth rib (a thoracotomy).

But there are risks involved with existing surgeries — mainly because so many important vessels run alongside the esophagus.



"To do the procedure, you actually have to pull on those vessels that supply the brain," says Tallant.

Preventing proper blood flow to the brain decreases the amount of oxygen flowing to the brain. This can lead to serious problems for the patient including neurological damage or even death in some cases.

Tallant and her supervisor, Dr. Kathleen Linn, are now investigating another approach that's potentially safer. It involves entering the dog's chest cavity through the space between the first two ribs (a first intercostal space thoracotomy).

"The idea of this new approach is to try not have to move or occlude any of those vessels," explains Tallant.

The idea for Tallant's research project, which is supported by the WCVM's Companion Animal Health Fund, was actually developed after a patient died following a sternotomy.

This surgical option could reduce the amount of manipulation that vessels must undergo, improving the outcome of the surgery for the pet. It may also shorten recovery times, leading to less stress for the dog and less of an emotional and financial burden for the owners.

During her study, Tallant will examine computed tomography (CT) images to compare the location of anatomical structures within the chest cavity of different small breed dogs.

The two procedures — sternotomy and thoracotomy — will then be tested and compared on canine cadavers, all of which were euthanized for reasons unrelated to the study and donated to the WCVM. For each surgical approach, Tallant will measure the percentage of esophagus available with and without retraction of the important vessels.

Tallant says the new approach will likely be performed on the next patient requiring surgical esophageal foreign body removal since complications are no more likely than with the current procedure. Fortunately severe esophageal blockages are rare, and Tallant has yet to have another patient requiring this type of surgery.

How can owners like me prevent their dogs from swallowing items that they shouldn't? Tallant's advice: make sure your dog's balls, toys or chewing objects are all large enough so they can't be quickly swallowed.

"But dogs will be dogs," says Tallant.

As for my dog Maggie, pigs' hooves are no longer on the menu. They've been replaced with more durable and safer chew toys that won't lead to a potentially sticky problem.

Melissa Cavanagh of Winnipeg, Man., is a second-year veterinary student who is the WCVM's research communications intern for the summer of 2013.

Find takes scientists from cold sores to cancer

A few years ago, Dr. Vikram Misra and his research team were studying how herpes simplex virus (HSV) can determine when their host is stressed. The virus responds by reactivating and causing cold sores to recur on or around the lips of people infected with HSV.

June 26th, 2012 | By Robyn Thrasher

"As many already know from personal experience or observation, once someone gets a cold sore it never really goes away," explains Misra, a virologist and head of the Western College of Veterinary Medicine's Department of Veterinary Microbiology. "They go away for awhile, but then they come back — often during times of stress."

After HSV replicates in skin cells, it infects the sensory nerve cells that deliver sensations of pain and heat to the face, thereby becoming latent and effectively "hiding" from the body's immune system.

When a person becomes stressed from illness, emotional stress or something as simple as a sunburn, the virus reactivates, replicates and returns to the skin's surface to create a cold sore.

"What we've been trying to figure out is how the virus actually senses when a host is stressed," says Misra. "We know it's to the virus's benefit to desert a so-called sinking ship. But how does it know when the ship is sinking?"

To investigate this mystery, the team began looking for what could rouse the sleeping HSV in these nerve cells. That's when they found the two unique proteins that were eventually named Zhangfei and Luman after two famous characters in Beijing opera.

"We were the first to discover these proteins so we got to name them," says Misra. "They work at cross purposes to each other. Luman is a very powerful gene activator that turns on genes that help to alleviate stress. It also turns on HSV replication. Zhangfei, on the other hand, turns off stress genes when they are no longer needed, and it also suppresses HSV replication soothing the virus into a 'sleeping' state."

What's interesting is that Zhangfei can also suppress the growth of many cancer cells.

"The discovery illustrates really nicely how science is not linear," says Misra. "It's funny how you start working on one thing and you end up doing something completely different."

Over the years, the WCVM research group has studied Zhangfei more intensely and determined that it has several different functions, many of which may be useful for controlling cancer.

"It suppresses cell division in many tumour cells," explains Misra, adding that the protein also shuts down the stress response. And Zhangfei has no effect on healthy, normal cells – making it ideal as a potential cancer therapy.

Very few cells produce Zhangfei naturally. According to Misra, it's only present in mature neurons – cells that have been instructed by various signalling mechanisms to become nerve cells.



WCVM virologist Dr. Vikram Misra: "It's funny how you start working on one thing and you end up doing something completely different. David Stobbe

an inactivated virus is used as a vector to introduce the Zhangfei gene into tumour cells.

"But you can

induce other cells

to make Zhangfei

by delivering the

gene to them," he

explains. In the lab,

"It works extremely well at turning off the growth of cancer cells, rendering them more susceptible to chemotherapy and radiation treatment," says Misra. And, in some cases, Zhangfei can even induce death of the cancer cells.

Oncology research has gradually become a staple for Misra's team. Besides work being done by oncology resident Dr. Kirsty Elliot, PhD student Rupali is working on a side project that looks at the reliance of certain breast cancers on estrogen for growth. Estrogen binds to a receptor within the cell, allowing it to enter the nucleus. There it can turn on cell division, causing the tumour to grow.

In retaliation, breast cancer patients take tamoxifen, a drug that acts as a substitute for estrogen and results in cell growth arrest. Unfortunately, over a period of time, the cancer cells become resistant to the drug. That's where Zhangfei enters the picture.

"Zhangfei also shuts down responses to nuclear receptors — the gene activator that binds estrogen is one of them," Misra says. "So our hypothesis is that if we deliver Zhangfei to the estrogen-dependent breast cancer cells or to the tamoxifen-resistant cells, it will not only turn off the primary tumour, but it will also negate any resistance."

So far, the work with Zhangfei has been confined to the laboratory setting and it's unknown when the protein will be used to treat a live animal.

"The use of viral vectors for laboratory analysis is acceptable, but may be problematic for clinical therapy," says Misra. He adds that future studies will look at determining other methods to get cells to make Zhangfei.

"We plan to find out the cell signals required to turn on the expression of this protein and hopefully figure out ways to manipulate these mechanisms so Zhangfei may be used in the live patient."

Robyn Thrasher of Edmonton, Alta., is a third-year veterinary student at the WCVM. Robyn is a WCVM research communications intern as well as a summer student in the WCVM Veterinary Medical Centre during the summer of 2012.

Study sets standard for knee assessment

Wearing a knee brace is a simple and easy method to conservatively manage a knee injury in people. But how useful are these orthopedic devices in dogs that injure their knee joints?

July 17th, 2012 | By Robyn Thrasher

"Right now, there's no peer-reviewed research that actually shows they work even though there are a lot of claims that they do," says Dr. Rhea Plesman, a small animal surgery resident at the Western College of Veterinary Medicine (WCVM).

Along with her resident advisor, WCVM small animal surgeon Dr. Kathleen Linn, Plesman planned to investigate the effectiveness of the knee brace in dogs for her graduate research project.

But after reviewing previous research, Plesman realized that she first needed to develop a standardized, non-invasive method of evaluating the knee (or stifle) joint following rupture of the cranial cruciate ligament.

The most common orthopedic condition seen in veterinary medicine, rupture of the CCL in canine patients is similar to an ACL (anterior cruciate ligament) tear in people. The injury can occur at any age and in any breed or size of dog with Labrador retrievers being one of the more commonly affected breeds.

The CCL plays a key role in stabilizing a dog's stifle joint, and a rupture often presents as a degenerative process in dogs.

"Owners often observe a waxing and waning type of lameness," explains Plesman. "An affected dog will appear sore, improve for a time and then become sore again until the entire ligament completely ruptures."

After a complete tear, an immediate, non-weight bearing lameness can occur that may improve over time. Owners may notice their dog no longer sits squarely and may sit with their legs off to the side. If the ligaments of both knees are damaged, affected dogs may have trouble going up and down stairs and difficulty rising from a sitting position.

Some patients may be medically managed with antiinflammatory medications, exercise restriction and joint supplements. But most require surgical intervention followed by physical rehabilitation in order to regain as much function of the stifle as possible.

Repeat radiographic techniques

When the CCL ruptures, the tibia moves forward in relation to the femur creating instability — a condition called cranial tibial subluxation (CTS).

"The current method of measuring CTS involves surgically implanting metal markers directly into the femur and tibia allowing for easy visualization on an X-ray," says Plesman. "But this isn't an ideal procedure for the live patient."



nent (CCL) rupture. Debra Marshall

There are several physical exam findings that also help to diagnose CCL rupture: both the cranial drawer test and the cranial tibial thrust test assess the amount of forward movement of the tibia in relation to the femur. As well, the presence of thickened fibrous tissue surrounding the knee joint and fluid build-up within the joint capsule may indicate ligament rupture.

Radiographs are a helpful diagnostic tool, but Plesman found current techniques and measurements to be poorly defined and not standardized. With her study, the small animal surgery resident aimed to develop a repeatable radiographic technique for assessing CTS in clinically affected dogs.

With funds provided by the Canadian Kennel Club (CKC) and the veterinary college's Companion Animal Health Fund (CAHF), Plesman analyzed 10 randomly selected clinical cases of cranial cruciate ligament rupture that presented to the WCVM's Veterinary Medical Centre between 2010 and 2011.

With the help of Dr. Ajay Sharma, a board-certified radiologist and former WCVM associate professor of medical imaging, Plesman identified a series of radiographic landmarks on the femoral and tibial bones that showed potential to serve as points for measuring CTS.

"We chose landmarks that were easily seen on an X-ray," she says. "We also chose points that wouldn't be obscured by arthritic changes as well as points of reference commonly used for guiding surgical repair."

In the end, the research team chose six anatomical landmarks: two near the end of the femur and four at the top of the tibia.

Over the span of a year, Plesman collected 20 normal hind limbs from medium to large breed canine cadavers. With all of the tissues above the stifle joint cleared away, the limb was inserted into a custom-made limb press testing apparatus. To mimic normal weight bearing, a load equal to 20 per cent of the dog's body weight was applied to the leg using this apparatus.

For each specimen, radiographs were taken before and after cutting the cranial cruciate ligament, with and without the metal bone markers in place.

Plesman, Sharma and Dr. Peter Gilbert, a WCVM associate professor of small animal surgery, examined the radiographs and measured each landmark in relation to each other.

Measurements with the ligament intact were compared to measurements with the ligament cut to determine how much the tibia moved forward. As well, comparisons were made between the selected anatomical landmarks versus the metal bone markers.

The best of the bone markers

After assessing variability, the team concluded that the measurement of CTS from the caudal limit of the intercondylar fossa (a deep notch at the end of the back of the femur) to the intercondylar eminence (a raised ridge at the top of the tibia) was the most reliable. Both of these bony landmarks are near the attachment site for the cranial cruciate ligament.

Unexpectedly, the researchers observed a poor correlation between the anatomic landmarks and the bone markers.

"It's unusual since the use of these bone markers is considered the current gold standard for CTS measurement," says Plesman. She adds that this may have occurred for any number of reasons including the effects of internal rotation of the knee when the cranial cruciate ligament is ruptured.

The two-year study's results offer an improved method of radiographically diagnosing cruciate rupture. But more importantly, it significantly advances veterinary research related to cruciate disease.

"It offers some building blocks for future clinical studies," says Plesman. "It will also help to better evaluate the methods we're using to treat cruciate ruptures. We can assess the stifle postoperatively and figure out if there's something we could be doing better."

With this preliminary work behind them, the research team has begun the next phase in collaboration with Dr. James Johnston, an assistant professor in the University of Saskatchewan's College of Engineering. Johnston will play an important role in the design and testing of a tibial compression device that the research team hopes to use on a live dog.

The device will mimic the cranial tibial thrust test that veterinarians currently perform manually, essentially standardizing it so the same pressure and technique is used every time.

"We also want to develop a method of taking standing radiographs of the stifle," says Plesman.

With the knowledge gained from these investigations, the team can then start to look more intensively at the effectiveness of supportive stifle braces for dogs with cruciate ligament injuries.

"We hope to assess affected dogs using the tibial compression device before and after applying the brace," says Plesman. "It will be interesting to see if the brace provides stability and eliminates tibial thrust as many marketers claim."

Robyn Thrasher of Edmonton, Alta., is a third-year veterinary student at the WCVM. Robyn is a WCVM research communications intern as well as a summer student in the WCVM Veterinary Medical Centre during the summer of 2012.

Breathtaking therapy for spinal cord injuries

A spinal cord injury can have devastating, lifelong effects on an animal's or person's ability to breathe or move.

September 7th, 2011 | By Robyn Thrasher

Recovery from such an injury depends heavily on several factors including the type, severity and location of the damage. Sadly, other than rehabilitation exercises, there aren't a lot of successful therapies available to promote recovery.

"Much of the recovery that does happen is through plasticity – the nervous system's ability to adapt and take over the function of damaged regions," says Dr. Gillian Muir, a professor of neuroscience at the Western College of Veterinary Medicine (WCVM).

If connections between the spinal cord and the brain are completely severed, there is no chance of functional recovery. With a partial injury, changes within the nervous system can result in intact pathways taking over the function of lost connections.

Muir and her WCVM research team have focused their research efforts in this particular area over the past 10 years.

"Overall, I've been interested in examining how animals recover from nervous system damage," says Muir. "I'm curious about the recovery of their motor skills and how undamaged pathways can compensate for the loss of damaged ones."

The low-down on low oxygen levels

Since 2008, Muir has been investigating the effects of a novel, non-invasive treatment known as intermittent hypoxia on recovery of forelimb function following a partial spinal cord injury.

Intermittent hypoxia (IH) is a procedure in which subjects are alternately exposed to brief periods of low oxygen levels (hypoxia) and normal oxygen levels (normoxia).

Although the mechanism of this therapy is unknown, it's proposed that brief periods of oxygen deprivation cause an increase in the levels of serotonin within the spinal cord. Serotonin is a neurotransmitter chemical that's found primarily in the central nervous system. Higher levels of serotonin result in increased amounts of a protein known as brainderived neurotrophic factor (BDNF) that strengthens existing connections between the brain and spinal cord.

Muir first learned of this new treatment while on sabbatical at the University of Wisconsin-Madison (UW). She worked closely with Dr. Gordon Mitchell, a professor of neuroscience at the UW School of Veterinary Medicine who had been using the technique to assess its effects on recovery of breathing following spinal injury in the neck.

Mitchell found that breathing improved with the treatment. "Giving periods of low oxygen causes an animal to become hypoxic which results in an increased drive to breathe," explains Muir. "It drives the whole system to work harder."

IH: option for forelimb recovery?

Mitchell's success made Muir wonder if intermittent hypoxia could aid in the recovery of forelimb action since motor neurons (cells of the nervous system) associated with diaphragm movement are intermingled with some of the motor neurons that innervate the muscles of the forelimb.

After she returned to the WCVM, Muir began conducting experiments that exposed rats to this new, promising treatment.

Every day for a week, Muir's team watched uninjured rats run across a horizontal ladder with two-millimetre wire rungs spaced equally two centimetres apart.

The rats were evaluated on the same task four weeks after undergoing a spinal injury in the neck. Those that appeared to have had sufficient injury were accepted into the intermittent hypoxia trial.

One group of rats was exposed to five minutes of 20 per cent oxygen (the amount in room air) followed by five minutes of only 11 per cent oxygen. This exercise was repeated 10 times per session with one session occurring each day for seven days.

A second group of rats (the control group) was exposed to continuous levels of 20 per cent oxygen.

Each group's performance on the ladder task was recorded once per week after the treatment for four weeks.

"We looked at the number of times their feet slipped through the space between the rungs and how they gripped the rungs," says Muir.

Preliminary results showed that the treatment improves recovery of limb function when comparing the number of errors made before and after the therapy.

Irregular- vs. regular-spaced ladders

However, Muir's team has received some criticism on their protocol.

"We use ladders with regularly-spaced rungs while other researchers argue that ladders with irregularly-spaced rungs should be used to determine if there's a real improvement or not," explains Megan Wilson, a third-year veterinary student at the WCVM who worked in Muir's lab this summer on a study to justify the use of regularly-spaced ladders.

Some investigators reason that irregularly-spaced rungs or patterns that change each session are necessary to challenge the animal. "It's based on the idea that the animals, as they repeatedly crossed a ladder, would actually learn the pattern of the rungs and become better at it through practice," says Muir.

Wilson's project involved three groups of rats: one set used a regular ladder, the second set used an irregular ladder and the third set used an irregular ladder with a pattern that changed daily.

The rats' performances in each group were compared before and

after spinal injury. Wilson's data reveals that the rats don't make any more errors on an irregular versus a regular ladder, nor do they learn the pattern.

"It's worthwhile to repeat the study, but so far, there are no significant differences between the types of ladders used," says Wilson, who travelled to the University of Florida to present her research work at the Merial Veterinary Scholars Symposium in August.

Backed by Wilson's results, there's now evidence that Muir's method of using a regular ladder for the experiments is sound — allowing her to continue her investigations without doubt.

The WCVM team is now looking at the effectiveness of intermittent hypoxia for improving the ability to perform other tasks such as walking on a treadmill and gripping a wire grid.

Intermittent hypoxia can definitely be applied to spinal-injured pets, but the ultimate goal is to develop it as a human therapy.

While Muir and Mitchell have been doing a number of rat studies, a third member of the collaborative group, Dr. Randy Trumbower – an assistant professor in the department of rehabilitation medicine at the Emory School of Medicine in Atlanta, Ga. – has been using the technique with human volunteers.

"This treatment will have to be added in with physical rehabilitation therapy," says Muir. "Treadmill training and weight supported training are effective techniques that can go a certain extent. Our goal is to promote further recovery by using intermittent hypoxia in conjunction with rehab."

This partnership in translational research has been funded primarily by the U.S. Department of Defense's Congressionally Directed Medical Research Programs and the Craig H. Neilson Foundation.

Their innovative research, which also earned the principal investigators a prestigious research award in the U.S. last year, still requires further exploration. Not only does the mechanism of how the treatment works need to be confirmed, but the essential elements of the therapy must be established.

"We have to figure out if it's really necessary to expose subjects to intermittent hypoxia for seven days or if we really need to do five-minute intervals," explains Muir. "We want to work out the characteristics of the treatment so we can minimize the amount of intervention, but yet maximize the output."

But there's still so much to learn about intermittent hypoxia and Muir is wary of creating false hope about the treatment and its long-term effects. "More research is needed. The spinal cord is so complicated — the whole nervous system is complicated," she cautions. "We just don't know enough yet."

Robyn Thrasher of Edmonton, Alta., is a second-year veterinary student at the WCVM. Thrasher produced stories about the veterinary college's research program and its researchers as part of her summer job in research communications.



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